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ORIGINAL ARTICLE

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Osteosarcopenia is a potential predictor for the prognosis of patients who underwent hepatic resection for colorectal liver metastases

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Abstract

Aim: We investigated the prognostic impact of osteosarcopenia, which is the combination of osteopenia and sarcopenia, in patients with colorectal liver metastases (CRLM) after hepatic resection.

Methods: One hundred and eighteen patients were analyzed retrospectively. Osteopenia was evaluated with computed tomographic measurement of pixel density in the midvertebral core of the 11th thoracic vertebra. Sarcopenia was evaluated with psoas muscle areas at the third lumbar vertebra. Osteosarcopenia was defined as the concomitant occurrence of osteopenia and sarcopenia.

Results: Osteosarcopenia was identified in 38 (32%) of the patients. In univariate analysis, the overall survival was significantly worse in patients with lymph node metastases ($P = .01$), extrahepatic lesion ($P = .01$), sarcopenia ($P = .02$), osteosarcopenia ($P < .01$), Glasgow Prognostic Score (GPS) 1 or 2 ($P = .05$), and curability R 1 or 2 ($P = .04$). In multivariate analysis, lymph node metastases ($P < .01$), osteosarcopenia ($P < .01$), and GPS 1 or 2 ($P = .03$) were independent and significant predictors of the overall survival. In patients with osteosarcopenia, there were more women than men and body mass index was lower compared to patients without osteosarcopenia.

Conclusion: Osteosarcopenia was the strong predictor for outcomes in patients who underwent liver resection for CRLM.

KEYWORDS

colorectal liver metastases, liver resection, osteopenia, osteosarcopenia, sarcopenia

1 | INTRODUCTION

Colorectal cancer is the third most common cancer worldwide, with a yearly increase in incidence.[1] Of these, 20%–25% of patients will have colorectal liver metastases (CRLM) at presentation and a further 40%–50% will develop metachronous CRLM after primary tumor resection.[2] Hepatic resection is the only treatment that can provide the possibility of prolonged survival for patients with CRLM, and their 5-year survival rate has reached 30%–50%.[3]

Sarcopenia was introduced as an age-related involuntary loss of muscle mass in 1989.[4] Recently, sarcopenia is defined as a complex syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength.[5] Sarcopenia can predict survival in patients with various kinds of cancer or patients with liver cirrhosis[6–8] and has been identified as a factor that indicates a poor prognosis after liver resection, including hepatocellular carcinoma (HCC), intrahepatic cholagiocarcinoma, and CRLM.[9–11]

Sarcopenia has been linked to low bone mineral density (BMD), known as osteopenia, suggesting that a low muscle mass decreases the mechanical loading on the skeleton, leading to reduced bone formation.[12] Sharma et al[13] demonstrated that low BMD was independently associated with post-liver transplantation mortality in HCC patients.

Recently, the concept and term "osteosarcopenia" has been established, which is defined as the concomitant occurrence of sarcopenia and osteopenia.[14] Osteosarcopenia, described as a "hazardous duet," has more negative impacts on health-related quality of life and eventual prognosis, with an increased risk of falls, fractures, institutionalization, and mortality than sarcopenia and osteopenia alone. However, the impact of osteosarcopenia on the prognosis for malignancies has not been reported yet.

The aim of this study is to investigate the impact of preoperative osteosarcopenia on the outcomes of patients with CRLM after hepatic resection in conjunction with other nutritional markers including sarcopenia and osteopenia, as well as inflammatory parameters.

2 | METHODS

2.1 | Patients

Between May 2007 and October 2017, 118 consecutive patients with CRLM underwent initial hepatic resection at the Department of Surgery, Jikei University Hospital, Tokyo, Japan. We performed a retrospective review of a prospectively maintained database of patients. This study was approved by the Ethics Committee of the Jikei University School of Medicine (27-177).

2.2 | Treatment and patient management

All patients with no unresectable extrahepatic tumor underwent hepatic resection regardless of the size, number, or location of liver metastases as long as curative resection would leave sufficient remnant liver. Generally, parenchymal-sparing hepatectomy was performed and extent of hepatic resection was determined based on retention rate of indocyanine green at 15 minutes (ICG_{R15}). Percutaneous transhepatic portal embolization was performed for patients with estimated residual hepatic volume of less than 30%.

SSI was defined as a condition where purulent discharge was observed with or without microbiological evidence in the incision or in an organ or space. Organ or space infection was determined by radiologic evidence of a fluid collection necessitating antibiotic therapy or drainage.

Recurrence of colorectal cancer after hepatic resection for CRLM was defined as newly detected local, hepatic, lung or extrahepatic tumors by ultrasonography, contrast-enhanced computed tomography (CT), or gadoxetic acid-enhanced magnetic resonance imaging (EOB-MRI) with or without increase in serum carcinoembryonic antigen (CEA) or carbohydrate antigen 19-9 (CA19-9). For recurrent liver metastasis, repeated hepatic resection or systemic chemotherapy was performed. For lung metastasis, limited partial lung resection or systemic chemotherapy was performed. For local recurrence, tumor resection, radiotherapy, or systemic chemotherapy was performed. As with systemic chemotherapy, the patients received infusional 5-fluorouracil/l-leucovorin with oxaliplatin (FOLFOX) and/or infusional 5-fluorouracil/l-leucovorin with irinotecan (FOLFIRI).

2.3 | Definition of osteopenia, sarcopenia, and osteosarcopneia

Osteopenia was defined as actual bone mineral density (BMD) below the calculated standard BMD, which was calculated as previously reported[15] (308.82-2.49 × age in men and 311.84-2.41 × age in

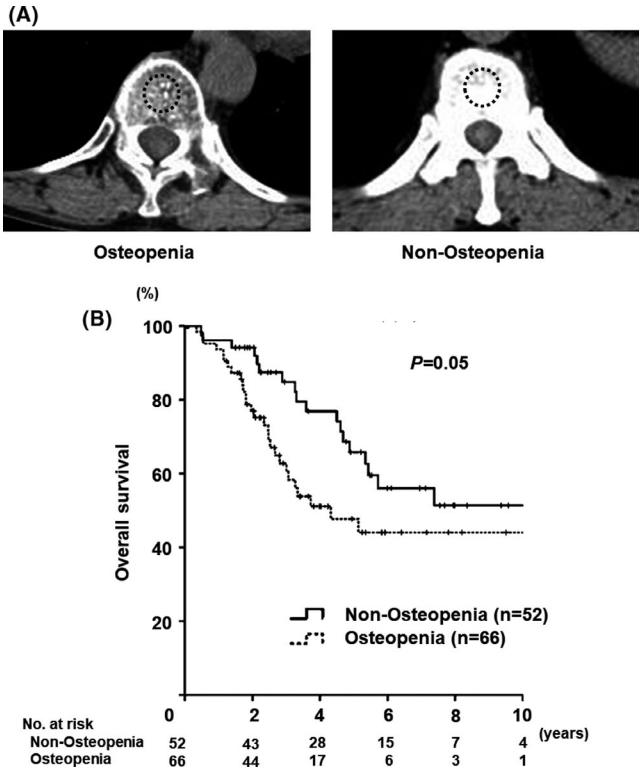

FIGURE 1 (A) Measurement of bone mineral density (BMD) on trabecular bone with calculation of the average pixel density within a circle in midvertebral core at 11th thoracic vertebral level. (B) Kaplan-Meier curve for overall survival after hepatic resection for colorectal liver metastases

women). BMD was measured in trabecular bone by calculating average pixel density within a circle in midvertebral core at the bottom of 11th thoracic vertebra (Th11) on preoperative CT[13] (Figure 1A). Sarcopenia was defined as psoas muscle mass area (PMA) below the established sex-specific median size and PMA was calculated using the formula (radii of the major axes × radii of the minor axes × π) at the level of the third lumber vertebra[10] (Figure 2A). Osteosarcopenia was defined as the concomitant occurrence of osteopenia and sarcopenia.

2.4 | Nutrition and inflammation markers

Hemogram and chemistry profile were measured preoperatively. The nutrition and inflammation-based biomarkers examined in this study were the following: Glasgow Prognostic Score (GPS), which is a combination of C-reactive protein (CRP) and albumin (Alb); patients with a normal Alb level (≥3.5 mg/dL) and a normal CRP level (<10 mg/L) were allocated a score of 0, patients with a low Alb level (<3.5 mg/dL) or an elevated CRP (≥10 mg/L) were allocated a score of 1, and patients with both a low Alb level (<3.5 mg/dL) and an elevated CRP (≥10 mg/L) were allocated a score of 2[16]; prognostic nutritional index (PNI) which is calculated by the formula 10 × Alb (g/dL) + 0.005 × lymphocyte count/μL,[17] neutrophil-lymphocyte ratio (NLR)[18]; and platelet-lymphocyte ratio (PLR).[19]

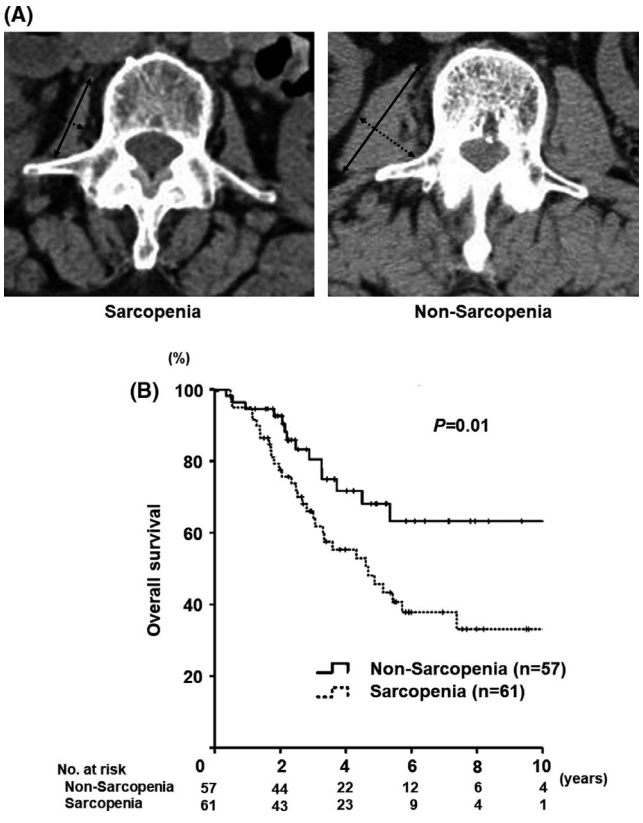

FIGURE 2 (A) Measurement of psoas muscle mass are (PMA) at third lumbar vertebral level by radii of the major axes (continuous line) × radii of the minor axes (dotted line) × π. (B) Kaplan-Meier curve for overall survival after hepatic resection for colorectal liver metastases

2.5 | Analyses of risk factors for recurrence and overall survival

We investigated the relation between clinicopathologic variables and disease-free or overall survival after initial liver resection by univariate and multivariate analyses. The variables include diabetes mellitus, cardiovascular disease, alcohol drinking, smoking, regional lymph node metastases of primary colorectal cancer, timing of tumor (synchronous or metachronous CRLM), neoadjuvant chemotherapy, tumor number, tumor size, extrahepatic lesion, osteopenia, sarcopenia, osteosarcopenia, GPS, PNI, NLR, PLR, serum CEA level, and curability (R1, 2 or R0). Continuous variables were classified into two groups for the Cox proportional hazard regression model based on the previous literature as follows: tumor size ≥50 or <50 mm,[20] PNI ≥ 45 or <45,[21] NLR ≥ 3 or <3,[22] PLR ≥ 150 or <150[23] and serum CEA ≥ 20 or <20 ng/mL.[20]

Next, we investigated the relation between clinical variables and osteosarcopenia by univariate analysis. The variables include age, gender, body mass index, diabetes mellitus, cardiovascular disease, regional lymph node metastases of primary colorectal cancer, timing of tumor, neoadjuvant chemotherapy, extrahepatic lesion, tumor number, BMD, PMA, GPS, PNI, NLR, PLR, operation time, intraoperative blood loss, postoperative SSI, adjuvant chemotherapy, and treatment for recurrence.

2.6 | Statistical analysis

The data were expressed as the median (inter quartile range). Univariate analysis were performed using the Mann-Whitney *U* test and chi-square test. Univariate and multivariate analyses of disease-free and overall survival was performed using the Cox proportional regression model. Survival curve was calculated using the Kaplan-Meier method with the Log-rank test. All *P*-values were considered statistically significant when the associated probability was less than .05.

3 | RESULTS

3.1 | Patient characteristics

The mean age was 67.5 years with a range 28-90 years. The median value of BMD was 139 Hounsfield units (HU) and osteopenia was diagnosed in 66 patients (56%) according to the calculated standard BMD values. The median PMA was 23.1 cm^2 for men and 11.9 cm^2 for women and sarcopenia was diagnosed in 61 patients (52%) and osteosarcopenia was diagnosed in 38 patients (32%). In this study, the 3-year disease-free and overall survival rate after hepatic resection for CRLM was 28.7% and 71.5%, respectively.

TABLE 1 Univariate and multivariate analyses of clinicopathological variables in relation to disease-free survival after hepatic resection for colorectal liver metastases

		DFS univariate analysis		DFS multivariate analysis	
Variables	**N**	**Hazard ratio (95% CI)**	***P*-value**	**Hazard ratio (95% CI)**	***P*-value**
Lymph node metastases					
Yes	74	1.68 (1.04-2.69)	.03	1.52 (0.93-2.49)	.09
No	44				
Timing of tumor					
Synchronous	74	1.37 (0.86-2.18)	.18		
Metachronous	44				
Neoadjuvant chemotherapy					
Yes	41	1.37 (0.88-2.15)	.17		
No	77				
Tumor number					
Multiple	61	1.99 (1.28-3.11)	<.01	2.06 (1.31-3.23)	<.01
Solitary	57				
Tumor size, mm					
≥50	25	0.93 (0.54-1.61)	.79		
<50	93				
Extrahepatic lesion					
Yes	19	2.10 (1.21-3.64)	<.01	2.53 (1.44-4.44)	<.01
No	99				
Osteopenia					
Yes	66	1.30 (0.83-2.01)	.25		
No	52				
Sarcopenia					
Yes	61	1.53 (0.98-2.39)	.06		
No	57				
Osteosarcopenia					
Yes	38	1.42 (0.90-2.23)	.13		
No	80				
GPS					
1 or 2	31	1.35 (0.83-2.20)	.22		
0	87				
PNI					
≥45	66	0.78 (0.50-1.20)	.26		
<45	52				
NLR					
≥3	38	1.29 (0.82-2.03)	.28		
<3	80				
PLR					
≥150	58	1.59 (1.03-2.47)	.04	1.64 (1.04-2.59)	.04
<150	60				
Serum CEA, ng/mL					
≥20	46	1.32 (0.85-2.05)	.22		
<20	72				
Curability					
R1 or 2	16	1.80 (0.99-3.29)	.05		
R0	102				

Abbreviations: CEA, carcinoembryonic antigen; CI, confidence interval; DFS, disease-free survival; GPS, Glasgow Prognostic Score; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; PNI, prognostic nutrition index.

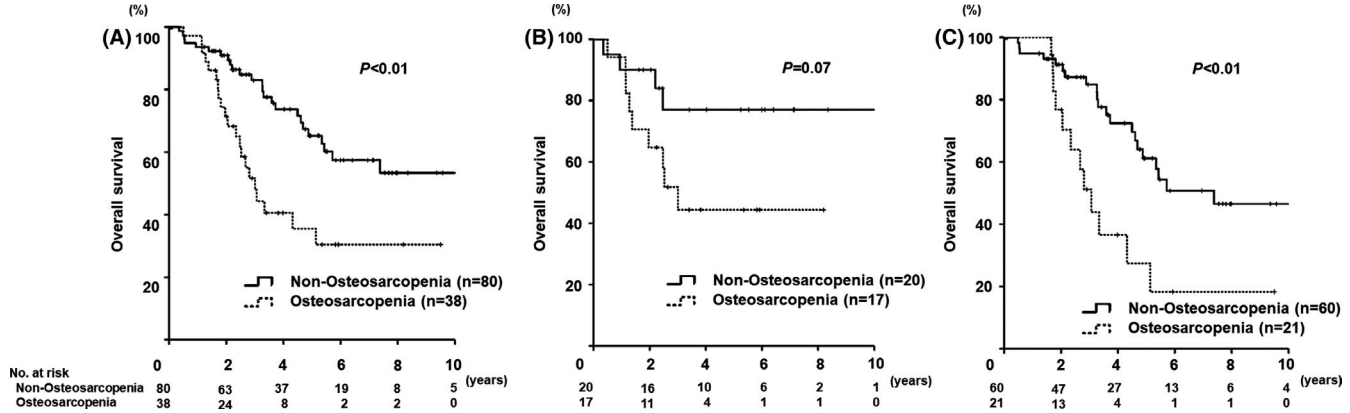

FIGURE 3 Kaplan-Meier curve for overall survival after hepatic resection for colorectal liver metastases among (A) all patients, (B) women, and (C) men

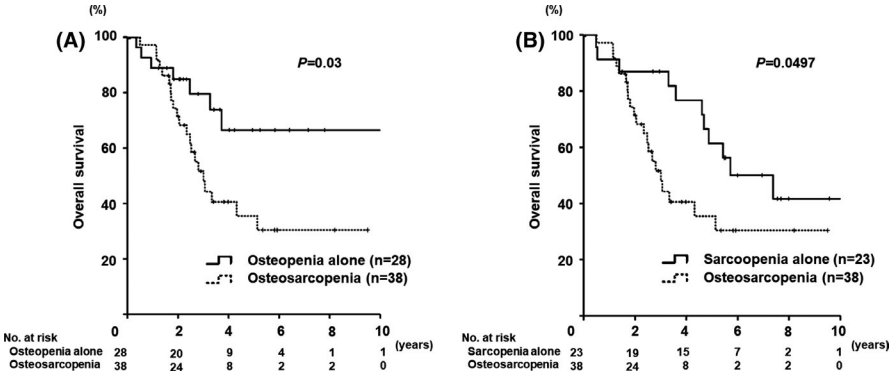

FIGURE 4 Kaplan-Meier curve for overall survival after hepatic resection for colorectal liver metastases in (A) patients with osteopenia alone (B) patients with sarcopenia alone compared to patients with osteosarcopenia

3.2 | Univariate and multivariate analyses of clinicopathological variables in relation to disease-free survival after hepatic resection for CRLM

Table 1 lists the association between the clinicopathological variables and disease-free survival after hepatic resection for CRLM. In univariate analysis, the disease-free survival was significantly worse in patients with lymph node metastases ($P = .03$), multiple tumors ($P < .01$), extrahepatic lesion ($P < .01$), and PLR ≥ 150 ($P = .04$). In multivariate analysis, multiple tumors (hazard ratio 2.06, 95% confidence interval 1.31-3.23, $P < .01$), extrahepatic lesion (hazard ratio 2.53, 95% confidence interval 1.44-4.44, $P < .01$), and PLR ≥ 150 (hazard ratio 1.64, 95% confidence interval 1.04-2.59, $P = .04$) were independent and significant predictors of the disease-free survival.

3.3 | Impact of osteopenia, sarcopenia, and osteosarcopenia for overall survival after hepatic resection for CRLM

The overall survival of patients with osteopenia was significantly lower than that of patients without osteopenia ($P = .05$; 3-year survival, 60.5% vs 82.2%) (Figure 1B). The overall survival of patients with sarcopenia was significantly lower than that of patients without sarcopenia ($P = .02$; 3-year survival, 63.9% vs 77.7%) (Figure 2B). The overall survival of patients with osteosarcopenia was significantly lower than that of patients without osteosarcopenia ($P < .01$; 3-year survival, 47.9% vs 81.2%) (Figure 3A). The Kaplan-Meier curve separated by gender showed that male patients not female patients with osteosarcopenia had significantly worse overall survival than those without osteosarcopnenia ($P < .01$, $P = .07$, respectively) (Figure 3B,C).

The overall survival of patients with osteosarcopenia was significantly lower than that of patients with osteopenia alone and sarcopenia alone ($P = .03$, .0497, respectively) (Figure 4).

3.4 | Univariate and multivariate analyses of clinicopathological variables in relation to overall survival after hepatic resection for CRLM

Table 2 lists the association between the clinicopathological variables and overall survival after hepatic resection for CRLM. In univariate analysis, the overall survival was significantly worse in patients with lymph node metastases ($P = .01$), extrahepatic lesion ($P = .01$), sarcopenia ($P = .02$), osteosarcopenia ($P < .01$), GPS 1 or 2 ($P = .05$), and R1 or 2 ($P = .04$). In multivariate analysis, lymph node metastases (hazard ratio 2.60, 95% confidence interval 1.26-5.38, $P < .01$), osteosarcopenia (hazard ratio 3.17, 95% confidence interval 1.38-7.25, $P < .01$) and GPS 1 or 2 (hazard ratio 2.11, 95% confidence interval

TABLE 2 Univariate and multivariate analyses of clinicopathological variables in relation to overall survival after hepatic resection for colorectal liver metastases

		OS univariate analysis		OS multivariate analysis	
Variables	**N**	**Hazard ratio (95% CI)**	***P*-value**	**Hazard ratio (95% CI)**	***P*-value**
Diabetes mellitus					
Yes	20	0.78 (0.31-1.99))	.61		
No	98				
Cardiovascular disease					
Yes	17	0.64 (0.25-1.62)	.34		
No	111				
Alcohol drinking					
Yes	10	0.84 (0.26-2.72)	.77		
No	108				
Smoking					
Yes	38	1.05 (0.57-1.95)	.87		
No	80				
Lymph node metastases					
Yes	74	2.43 (1.20-4.90)	.01	2.60 (1.26-5.38)	<.01
No	44				
Timing of tumor					
Synchronous	74	1.20 (0.64-2.24)	.58		
Metachronous	44				
Neoadjuvant chemotherapy					
Yes	41	1.77 (0.99-3.19)	.06		
No	77				
Tumor number					
Multiple	61	1.50 (0.83-2.70)	.18		
Solitary	57				
Tumor size, mm					
≥50	25	1.32 (0.67-2.61)	.42		
<50	93				
Extrahepatic lesion					
Yes	19	2.28 (1.18-4.40)	.01	1.84 (0.93-3.65)	.08
No	99				
Osteopenia					
Yes	66	1.81 (0.99-3.29)	.05		
No	52				
Sarcopenia					
Yes	61	2.13 (1.14-4.00)	.02	0.95 (0.41-2.21)	.91
No	57				
Osteosarcopenia					
Yes	38	2.54 (1.41-4.56)	<.01	3.17 (1.38-7.25)	<.01
No	80				
GPS					
1 or 2	31	1.86 (1.00-3.45)	.05	2.11 (1.06-4.20)	.03
0	87				
PNI					

(Continues)

TABLE 2 (Continued)

Variables	N	OS univariate analysis		OS multivariate analysis	
		Hazard ratio (95% CI)	*P*-value	Hazard ratio (95% CI)	*P*-value
≥45	66	0.59 (0.33-1.06)	.08		
<45	52				
NLR					
≥3	38	1.47 (0.82-2.64)	.20		
<3	80				
PLR					
≥150	58	1.31 (0.73-2.34)	.36		
<150	60				
Serum CEA, ng/mL					
≥20	46	1.52 (0.85-2.72)	.16		
<20	72				
Curability					
R1 or 2	16	2.30 (1.02-5.18)	.04	2.21 (0.96-5.10)	.06
R0	102				

Abbreviations: CEA, carcinoembryonic antigen; CI, confidence interval; GPS, Glasgow Prognostic Score; NLR, neutrophil-lymphocyte ratio; OS, overall survival; PLR, platelet-lymphocyte ratio; PNI, prognostic nutrition index.

1.06-4.20, $P < .01$) were independent and significant predictors of the overall survival.

3.5 | Association between clinical variables and osteosarcopenia

Table 3 lists the association between clinical variables and osteosarcopenia. In patients with osteosarcopenia, female patients were significantly more common and body mass index, BMD, and PMA was significantly lower compared to patients without osteosarcopenia ($P = .03$, <.01, <.01 and <.01, respectively). GPS, PNI, NLR,PLR, adjuvant chemotherapy, and treatment for recurrence were comparable between the two groups.

4 | DISCUSSION

In the present study, we evaluated the impact of preoperative osteosarcopenia on the outcomes after hepatic resection for CRLM. To the best of our knowledge, this is the first report to demonstrate the impact of preoperative osteosarcopenia on prognosis for malignancies and to compare with other preoperative nutritional predictors of prognosis, including GPS, PNI, NLR, PLR, and patients' status of sarcopenia and osteopenia. Multivariate analysis using the Cox proportional regression model showed that osteosarcopenia was independently associated with poor overall survival after hepatic resection for CRLM. And overall survival in patients with osteosarcopenia was significantly worse those with sarcopenia alone or osteopenia alone.

Sarcopenia plays an important role as a prognostic factor for various tumors. Inflammatory conditions, nutritional factors, and aging have been postulated as the molecular mechanism. On the other hand, there are few reports to show the prognostic value of osteopenia.[13,15] It is not clear whether the bone loss promotes cancer development or whether stable bone density prevents cancer invasion. Gender, low body mass index, comorbidities, such as diabetes and kidney dysfunction, low levels of Vitamin D, reduced insulin-like growth factor-1, and malnutrition have been associated with osteosarcopenia.[24] Our findings showed that in patients with osteosarcopenia, female patients were significantly more common and body mass index was significantly lower compared to patients without osteosarcopenia. On the other hand, there were no differences in comorbidities (diabetes and cardiovascular disease), serum creatinine level (0.77 vs 0.79 mg/dL; $P = .32$), serum calcium level (9.2 vs 9.1 mg/dL; $P = .44$), serum Alb level (3.9 vs 3.8 g/dL; $P = .72$), serum prealbumin level (23.6 vs 23.9 mg/dL; $P = .59$), serum transferrin level (227 vs 245 mg/dL; $P = .17$), and serum retinol-binding protein level (2.8 vs 2.9 mg/dL; $P = .49$) including the nutrition and inflammation-based biomarkers such as GPS, PNI, NLR, and PLR between patients with and without osteosarcopenia. Chen et al[25] reported that women with a lower body weight at colorectal cancer diagnosis had an increased mortality risk, which is the same as the present study. According to the Kaplan-Meier curve separated by gender, the overall survival of female patients with osteosarcopenia was not significantly worse than that of female patients without osteosarcopenia. However, female patients with osteosarcopenia were likely to have poorer prognosis than those without osteosarcopenia ($P = .07$), and we could explain this discrepancy but the sample size was too small to show the statistical significance.

The BMD measurement is a surrogate cumulative exposure to multiple factors, including vitamin D and estrogen. Vitamin D and

TABLE 3 Univariate analysis of clinical variables in relation to osteosarcopenia

Variables	Osteosarcopenia		*P*-value
	Yes (n = 38)	No (n = 80)	
Age, y	68 (61-75)	66 (60-74)	.61
Gender, female	17 (45%)	20 (25%)	.03
Body mass index, kg/m^2	21 (19-23)	23 (21-25)	<.01
Diabetes mellitus	7 (18%)	13 (16%)	.77
Cardiovascular disease	6 (16%)	11 (14%)	.77
Lymph node metastases, yes	24 (63%)	50 (63%)	.94
Timing of tumor, synchronous	23 (61%)	51 (64%)	.74
Neoadjuvant chemotherapy, yes	14 (37%)	27 (34%)	.74
Extrahepatic lesion, yes	9 (24%)	10 (13%)	.12
Tumor number	1 (1-2)	2 (1-3)	.52
Tumor size, mm	27 (18-45)	26 (17-43)	.60
BMD, HU	113 (90-126)	156 (128-196)	<.01
PMA, cm^2	11 (10-19)	24 (18-30)	<.01
GPS, 1 or 2	9 (24%)	22 (28%)	.66
PNI	46 (40-49)	46 (42-49)	.58
NLR	2 (2-3)	2 (2-3)	.99
PLR	170 (121-211)	144 (101-206)	.11
Operation time, min	385 (275-469)	375 (290-475)	.90
Intraoperative blood loss, mL	340 (100-980)	495 (198-1.101)	.29
Postoperative SSI, yes	3 (8%)	12 (15%)	.30
Adjuvant chemotherapy, yes	25 (66%)	48 (60%)	.55
Treatment for recurrence (resection:locoregional therapy:chemotherapy: none)	10:0:15:5	20:3:21:8	.51

Abbreviations: BMD, bone mineral density; CEA, carcinoembryonic antigen; GPS, Glasgow Prognostic Score; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; PMA, psoas muscle mass area; PNI, prognostic nutrition index; SSI, surgical site infection.

estrogen have important roles not only in osteopenia but also in the development of colorectal cancer. Ng et al[26] reported that serum vitamin D was associated with a significant improvement in overall survival among patients with colorectal cancer. Rennert et al[27] reported that the use of hormone replacement therapy was associated with a 63% relative reduction of colorectal cancer in postmenopausal women. Another study demonstrated that young women with metastatic colorectal cancer had better overall survival than men.[28] The implication is that vitamin D and estrogen have a crucial biological role in cancer progression in colorectal cancer. Further investigations into the associations between vitamin D and estrogen profile, and osteosarcopenia in patients with CRLM, are needed.

Interestingly, in this study, there was no significant difference in the disease-free survival between the patients with and without osteosarcopenia. Toshima et al and Sharma et al also demonstrated that osteopenia was independently associated with post-liver transplantation survival in HCC patients, but not recurrence.[15,13] They pointed out how effective treatments for recurrence were done might be related to osteopenia; however, the present study showed that treatment for recurrence was comparable between them. In addition, most patients with osteosarcopenia (21/22 patients) died of colorectal cancer-related death (one patient died of interstitial pneumonia), which could suggest that osteosarcopenia only affected cancer-related death. This discrepancy should be investigated in the future.

Several limitations must be considered when interpreting the present findings. The study was retrospective and conducted in a single institution with a relatively small sample size. Our results should be confirmed in larger prospective studies. The prognostic impact of sarcopenia and osteopenia on survival for malignancies has been demonstrated in several studies. Although varying cutoff points regarding skeletal muscle mass and BMD have been used, the definitions of sarcopenia and osteopenia remain controversial, with a variety of claimed appropriate diagnostic cutoff values. In our study, we based the cutoff values on the median PMA of the population for sarcopenia and the standard BMD with age for osteopenia.

Interventions such as supportive therapy focusing on nutrition and rehabilitation would be applicable for patients with osteosaropenia to improve outcomes after hepatic resection for CRLM. Perioperative nutritional therapy such as synbiotics, micronutrients, branched-chain amino acid, and immunonutrition formulas in liver transplant recipients who have decreased skeletal muscle mass and malnutrition have been considered essential interventions to improve outcomes after liver transplantation.[29] For osteosarcopenia, vitamin D, calcium, osteoporotic drugs such as teriparatide, denosumab and bisphosphates, exercises are needed to improve musculoskeletal health.[14]

In conclusion, we demonstrated that preoperative osteosarcopenia was more closely related to postoperative survival than sarcopenia and osteopenia alone in patients who underwent hepatic resection for CRLM. The evaluation of skeletal muscle and BMD may be useful for risk stratification and clinical decision-making for patients with CRLM. Early interventions such as nutritional support and physical exercise may improve outcomes after hepatic resection for CRLM.

DISCLOSURE

Conflict of Interest: The authors have no conflicts of interest and funding to declare.

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