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Impact of Sarcopenia on Outcomes Following Intra-arterial Therapy of Hepatic Malignancies

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Abstract

Background—Assessment of patient performance status is often subjective. Sarcopenia—measurement of muscle wasting—may be a more objective means to assess performance status and therefore mortality risk following intra-arterial therapy (IAT).

Methods—Total psoas area (TPA) was measured on cross-sectional imaging in 216 patients undergoing IAT of hepatic malignancies between 2002 and 2012. Sarcopenia was defined as TPA in the lowest sex-specific quartile. Impact of sarcopenia was assessed relative to other clinicopathological factors.

Results—Indications for IAT included hepatocellular carcinoma (51 %), intrahepatic cholangiocarcinoma (13 %), colorectal liver metastasis (7 %), or other metastatic disease (30 %). Median TPA among men (568 mm²/m²) was greater than women (413 mm²/m²). IAT involved conventional chemoembolization (54 %), drug-eluting beads (40 %), or yttrium-90 (6 %). Median tumor size was 5.8 cm; most patients had multiple lesions (74 %). Ninety-day mortality was 9.3 %; 3-year survival was 39 %. Factors associated with risk of death were tumor size (HR=1.84) and Child's score (HR=2.15) (all $P < 0.05$). On multivariate analysis, sarcopenia remained independently associated with increased risk of death (lowest vs. highest TPA quartile, HR=1.84; $P = 0.04$). Sarcopenic patients had a 3-year survival of 28 vs. 44 % for non-sarcopenic patients.

Conclusions—Sarcopenia was an independent predictor of mortality following IAT with sarcopenic patients having a twofold increased risk of death. Sarcopenia is an objective measure of frailty that can help clinical decision-making regarding IAT for hepatic malignancies.

Keywords

Sarcopenia; Intra-arterial therapy; Frailty; Outcomes; Performance status

Introduction

Surgery remains the optimal treatment for hepatic malignancies including primary liver tumors, such as hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC), as well as metastatic lesions such as colorectal liver metastasis (CRLM) and neuroendocrine liver metastasis (NELM). Many patients, however, are not amenable to surgery due to disease extent, quality of the underlying hepatic parenchyma, or medical comorbidities.^{1–3} Hepatic intraarterial therapy (IAT) is an established therapeutic option for patients who have liver dominant disease that is not amenable to surgery. IAT takes advantage of the fact that hepatic neoplasms receive the majority of their blood supply from the hepatic artery compared with normal hepatocytes, which are primarily supplied by the portal vein.¹ IAT can involve bland embolization, transarterial chemoembolization (TACE), drug-eluting bead TACE (DEB TACE), or radioembolization (yttrium-90).^{4–6} IAT has been shown to be associated with a survival benefit in the treatment of primary and some secondary liver malignancies.^{7–13}

While IAT therapy is generally well tolerated, it can be associated with peri-procedural morbidity. High total bilirubin and poor patient performance status (PS) have both been associated with worse outcomes following IAT.^{14–19} In fact, PS is explicitly included in the Barcelona Clinic Liver Cancer (BCLC) staging system as a key criteria in directing treatment recommendations.²⁰ In addition, PS has been shown to be a comprehensive determinant of overall health status, an indicator of treatment response, and a predictor of long-term survival in cancer patients.^{21–24} PS is particularly relevant to decisions around IAT utilization as it has been shown to be an independent prognostic predictor of survival following hepatic IAT.^{14–19} Despite its prognostic importance, PS can be difficult to objectively define even with the use of tools such as the Lansky, Eastern Cooperative Oncology Group (ECOG), and Karnofsky performance status scores.^{21,25–28} Frailty has

been used as a surrogate of PS. Frailty is thought to estimate physiologic reserves and can be measured with subjective evaluations of cognition, weakness, exhaustion, and physical activity.^{29,30} More recently, our group and others have examined the use of muscle loss (sarcopenia) as a more objective measure of frailty and PS. The impact of sarcopenia has been investigated among patients receiving chemotherapy, as well as those undergoing various surgical procedures.^{31–38} To our knowledge, however, the impact of sarcopenia on short- and long-term outcomes following IAT has not been previously explored.

We herein sought to investigate the incidence of sarcopenia in patients undergoing IAT for hepatic malignancies. In addition, we investigated the impact of sarcopenia on both short- and long-term outcome among patients undergoing IAT for both primary and secondary malignancies of the liver. We hypothesize that sarcopenia may be associated with increased morbidity and worse long-term survival among patients undergoing IAT.

Methods

Patients and Data Collection

Between 2002 and 2012, patients who underwent hepatic IAT were identified from the Johns Hopkins Hospital liver database. Pretreatment (within 30 days of IAT) abdominal cross-sectional images were available for re-review for 216 patients, representing the study cohort. Clinical and pathological data were collected including information on demographics, tumor stage, tumor size, IAT details, IAT response, resectability, treatment interventions other than IAT, as well as hospital level details. Data on perioperative morbidity and mortality were also collected. Complications were scored by Clavien–Dindo classification with major complications being defined as Clavien grade 3.³⁹ The Johns Hopkins Institutional Review Board approved this study.

Image Analysis

As previously described,^{33,36} sarcopenia was assessed by measuring the cross-sectional area of the right and left psoas muscles (total psoas muscle area=TPA). TPA was measured at the level of L3 using the first image with both vertebral spines visible. Measurements were performed in a semi-automated fashion. First, the border of the psoas muscle was manually outlined. Next, the density threshold was set between –30 and 110 Hounsfield units (HU) (Fig. 1).³³ This allowed for automatic calculation of psoas muscle area by excluding vasculature and, more importantly, areas of fatty infiltration based on HU. All images were analyzed using Ultraview software package (Merge Emageon, Birmingham, AL, USA). The measured psoas area was then normalized for height, as per convention for body composition measurements (TPA in square millimeter/square meter).^{40–42}

Statistical Analysis

Data were reported as median and interquartile range (IQR), for continuous variables. The impact of sarcopenia was evaluated as both a continuous and categorical variable. Patients were stratified by quartiles according to TPA and sarcopenia was defined in the categorical analyses as the lowest quartile for men and women separately. The impact of sarcopenia on morbidity and mortality was examined using univariate and multivariate analyses. Overall survival was evaluated using the Kaplan–Meier method. A *P* value < 0.05 was considered statistically significant. Statistical analyses were performed using Stata (Stata Corp, College Station, TX, USA).

Results

Demographics and Clinical Characteristics

The clinical and pathological characteristics of 216 patients included in the study are outlined in Table 1. The average age of the study population was 60 years. There were 138 men (63.9 %) and 78 women (36.1 %) in the study population. Indications for IAT included HCC (50.5 %), ICC (13.0 %), CRLM (6.5 %), or other metastatic disease (30.1 %) (Table 2). IAT involved conventional chemoembolization (53.7 %), drug-eluting beads (39.8 %), or yttrium-90 (6.5 %). The median number of IAT treatments was 2 (range, 1 to 9). Median tumor size was 5.8 cm and most patients had multiple lesions (73.6 %). A subset of patients received some type of therapy prior to IAT ($n=82$). Among these patients, pre-IAT therapy consisted of hepatic resection ($n=29$, 13.4 %), systemic chemotherapy ($n=62$, 28.7 %), biologic therapy ($n=20$, 9.3 %), ablation ($n=10$, 4.6 %), and IAT at another institution ($n=8$, 3.7 %). Among this subset, there were two patients who had already undergone both hepatic resection and IAT. The median TPA was 515 mm²/m² after normalizing for patient height. When stratified by gender, the median adjusted TPA was statistically lower for women than for men (413 vs. 568 mm²/m², $P<0.001$; Fig. 2a). The lowest quartile TPA threshold for men was 477 vs. 338 mm²/m² for women. Age also tended to be associated with the incidence of sarcopenia as there was a trend toward decreasing TPA with increasing age (Fig. 2b). Sarcopenia was noted across a wide range of BMIs. Sarcopenia was less frequently observed, however, among obese patients with a BMI ≥ 30 kg/m². Of the 48 patients who had a BMI ≥ 30 kg/m², 7 (14.6 %) also had sarcopenia and therefore were characterized as having sarcopenic obesity. In contrast, among patients with a BMI < 30 kg/m², the incidence of sarcopenia was 32.0 %.

Impact of Sarcopenia

Of the 216 patients who underwent IAT for hepatic malignancy, 17 experienced at least one complication for an overall morbidity of 7.8 %. Most complications were minor; only three patients experienced a major (Clavien grade ≥ 3) complication, none of whom had sarcopenia. Morbidity after IAT was mostly associated with hepatic encephalopathy ($n=2$), nausea/vomiting ($n=2$), and biloma formation ($n=2$). The three major complications included acute hepatic failure and encephalopathy, pulmonary embolism, and systemic inflammatory response syndrome. The presence of sarcopenia was not associated with the risk of overall morbidity (OR=0.89, 95 % CI 0.28–2.86; $P=0.84$). Median hospital stay for the entire cohort was 1 day and did not differ among patients with versus without sarcopenia ($P=0.85$) (Table 3).

There were 22 deaths within 90 days, for a periprocedural mortality of 10.2 %; of these 7 (32 %) had sarcopenia. When analyzed as a categorical variable, patients with sarcopenia did not have a higher risk of 90-day mortality (no sarcopenia, 9.3 % vs. sarcopenia, 12.7 %; $P=0.44$). For the entire cohort, the median overall survival was 26.0 months; overall 3- and 5-year survival rates were 38.8 and 27.2 %, respectively. On univariate analyses, the presence of sarcopenia (lowest vs. highest quartile TPA) was associated with overall survival (HR=2.20, 95 % CI 1.15–4.30; $P=0.02$) (Fig. 3 and Table 4). In fact, among the largest subgroup—patients with HCC—there was a three times higher risk of death among patient with sarcopenia compared with patients without sarcopenia (HR=3.05, 95 % CI 1.26–7.49). Again, the effect of sarcopenia on outcome was more notable in men (HR=2.31, 95 % CI 1.08–4.95; $P=0.03$) than women (HR=2.08, 95 % CI 0.68–6.32; $P=0.20$). Other factors associated with survival on univariate analyses included tumor size (HR=1.84, 95 % CI 1.18–2.86; $P=0.01$), and a higher Child's score (HR=2.15, 95 % CI 1.34–3.43; $P<0.001$). Among patients with HCC, Child class was not associated with TPA quartile (Child class A: quartile 1, 64.0 % vs. quartile 2, 65.5 % vs. quartile 3, 60.0 % vs. quartile 4, 66.7 %;

$P=0.86$). After controlling for competing risk factors on multivariate analyses, sarcopenia remained independently associated with an increased risk of death (lowest vs. highest quartile TPA, HR=1.84; 95 % 1.03–3.64; $P=0.04$) (Table 4).

Discussion

IAT can be an important therapeutic option for patients with liver dominant primary and secondary hepatic malignancies who are not amenable to surgery. Prognosis following IAT is undoubtedly multifactorial and related not only to tumor-specific factors but also individual patient characteristics. Age, total bilirubin, AFP, tumor size and stage, portal vein thrombosis, as well as presence of ascites all have prognostic importance following IAT.^{43–48} In addition to these factors, PS has also been demonstrated to be an important predictor of periprocedural complications and mortality after IAT.^{14–19} The central role of PS in clinical decision-making for patients with hepatic malignancy is underscored by its formal incorporation into the BCLC treatment algorithm. However, accurate assessment and measurement of PS to quantify patient-level physiological status has been questioned. While clinical assessment of PS may be subjective, sarcopenia, which involves the quantitative measurement of TPA on cross-sectional imaging, may be a more objective measure of frailty and PS.^{32,33,36,49} The current study is important because it is the first, to our knowledge, that specifically examines the impact of sarcopenia among patients undergoing IAT. Although previous studies have examined sarcopenia relative to chemotherapy or surgical interventions,^{31,32,34,36,38,49} the current study provides novel data on sarcopenia and IAT. We report that sarcopenia was not associated with periprocedural morbidity following IAT, but was associated with both short- and long-term mortality. Specifically, patients with sarcopenia were noted to have both worse 3- and 5-year overall survival.

Many patients with malignancy experience involuntary weight loss from generalized anorexia, chemotherapy, or cancer-related cachexia from endogenous transmitters and inflammatory mediators. Cancer-related cachexia is a complex metabolic disorder characterized by prominent loss of skeletal muscle with or without loss of body fat due to cytokine-induced catabolism.⁵⁰ The presence of cancer cachexia is associated with poor treatment outcomes, increased toxicity, reduced survival, and diminished quality of life.⁵⁰ Sarcopenia is distinct from cancer-related cachexia and is broadly defined as muscle loss associated with normal aging.^{50,51} However, it includes muscle loss from oncologic and non-oncologic disease states including chronic medical disease and malnutrition.^{52–54} The measure of sarcopenia is specific to muscle mass, and not weight or BMI. In the current study, sarcopenia was determined by measuring the total area of the psoas muscle using cross-sectional imaging at the level of the third lumbar vertebra. Processes leading to sarcopenia include both decreased skeletal muscle anabolism and increased catabolism from inflammatory factors and other agents.⁵⁵ Ultimately, sarcopenia results in decreased muscle mass, strength, and function, which translate into decreased physical performance, disability, increased fall-related injuries, and frailty.⁵⁵

Recently, the use of sarcopenia to predict outcomes in cancer patients has received increasing attention. Sarcopenia has been associated with worse outcomes among patients treated with chemotherapy for pancreatic, breast, prostate, and renal cell cancer.^{31,34,37,38,56} In addition, sarcopenia has been noted to affect adversely surgical outcomes for patients undergoing surgery for melanoma, colorectal liver metastases, hepatocellular carcinoma, and pancreatic surgery.^{32,33,35,36} In our previous work, we reported on the effect of sarcopenia among 259 patients who underwent liver resection for colorectal liver metastasis.³⁶ In this study, patients with sarcopenia had longer hospital stays, a higher chance of an extended ICU stay, and an increased risk of postoperative complications. In a separate study looking at the effect of sarcopenia among patients undergoing

pancreaticoduodenectomy for pancreatic cancer, we failed to find that sarcopenia impacted short-term outcomes such as length of stay or morbidity.³³ In this latter study, while the presence of sarcopenia was not associated with the risk of morbidity, it did adversely impact long-term survival. In the current study, we similarly found that sarcopenia was not associated with the risk of IAT periprocedural complications, but did impact overall survival. The finding that sarcopenia was not associated with morbidity was probably multifactorial. IAT was very well tolerated and there were few complications; given the low overall morbidity, the current study may have been underpowered to see an affect of sarcopenia on morbidity and a larger cohort may be necessary to demonstrate a difference.

The prognostic affect of sarcopenia on receipt of chemotherapy and some surgical procedures has been previously defined, but its association with other procedures used to treat cancer patients is less defined. In the current study, we noted that sarcopenia had a strong association with survival following IAT, as patients in the lowest TPA quartile had a worse long-term outcome compared with those patients in the highest TPA quartile. In fact, patients with sarcopenia had a twofold increased risk of death compared with patients in the highest TPA quartile. As expected, tumor size was also associated with survival. Importantly, even on multivariate analyses after controlling for competing risk factors, sarcopenia remained an independent predictor of long-term mortality following hepatic IAT. Englesbe et al. had similarly reported a threefold increased risk of mortality in patients with sarcopenia undergoing liver transplantation (3-year survival was 26 vs. 77 % in patients with and without sarcopenia, respectively).³² In a separate study by Van Vledder et al., the authors noted a nearly twofold decrease in 3-year survival among patients undergoing liver resection for colorectal liver metastasis who had sarcopenia (34 vs. 65 % in patients with and without sarcopenia, respectively).⁴⁹ Similarly in our group's previous study that examined patients undergoing resection of pancreatic adenocarcinoma, we noted that sarcopenia was associated with a 63 % increased risk of death at 3 years.³³ Taken together, our data corroborate and validate the importance of sarcopenia as a valuable tool to risk stratify patients with regard to prognosis and survival. While the presence or absence of sarcopenia should not necessarily dictate therapy, it may be an important objective measure of patient frailty that can predict long-term outcome independent of tumor-specific factors.

The current paper had several limitations. Similar to our previous work, frailty parameters such as grip strength, walking speed, or levels of exhaustion were not captured due to the study's retrospective design.^{33,36} If these measures had been collected, it would have allowed a comparison of more subjective measures of frailty to sarcopenia. Our cohort was relatively small and included a mixed population in regard to type and indication for IAT. Indications for hepatic IAT included a majority for HCC, while a minority where due to ICC, CRLM, or other metastatic disease. Given the relative small sample size, we were not able to study the potential effect of sarcopenia in any particular subset of patients. It is possible, however, that the effect of sarcopenia may vary following IAT based on the underlying patient population and IAT indication. Finally, another source of variation in our cohort was type of IAT. Again, our cohort was comprised of patients who received various types of IAT; however, the majority of patients received either standard TACE or DEB TACE, while only a minority of patients received radioembolization.

In conclusion, surgical resection of hepatic malignancies remains the mainstay of treatment for most patients with potentially resectable liver disease; however, IAT is an important and frequently used modality of care that can have a survival benefit, as well as palliate symptoms. While much attention has been paid in the literature to tumor-specific factors that may be associated with prognosis, other patient-centered factors have not received as much attention. We herein highlight the potential importance of muscle mass measurement based on preoperative cross-sectional imaging. Specifically, we noted that loss of this muscle

mass, defined as sarcopenia, was associated with an increased risk of overall mortality and worse long-term outcomes following IAT. Similar to tumor-specific metrics of prognosis, pretherapy assessment of sarcopenia may be an important tool to inform clinical decision-making and assist in risk stratification of patients with hepatic malignancies undergoing IAT.

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Fig. 1.

Total psoas area (TPA) was measured at the level of L3 on the first image with both vertebral spines visible. Measurements were performed in a semi-automated fashion with manual outlining of psoas muscle borders and setting the density threshold between -30 and 110 Hounsfield units (HU) (From Peng et al.,³³ with permission)

Fig. 2.
a Distribution of total psoas area (TPA)/square meter stratified by gender; mean-adjusted TPA was statistically lower for women than men (413 vs. 568 mm²/m², $P < 0.001$). **b** Distribution of TPA/square meter according to age

Fig. 3. Overall survival stratified by **a** sarcopenia (TPA/square meter) and **b** TPA/square meter divided into quartiles. The presence of sarcopenia was associated with risk of death (lowest vs. highest quartile TPA, HR=2.20; $P=0.02$)

Table 1

Demographic and health-status-related characteristics of patients who underwent IAT for hepatic malignancies

	All patients (<i>n</i> = 216)	Men (<i>n</i> = 139)	Women (<i>n</i> = 77)	<i>P</i> value ^{<i>a</i>}
Age at IAT (years); median (IQR)	60 (54–67)	59 (54–67)	60 (51–66)	0.29
BMI (kg/m ²); median (IQR)	25.1 (22.2–29.7)	25.5 (23.1–30.0)	24.3 (20.7–28.7)	0.07
Total psoas area (mm ² /m ²); median (IQR)	515 (409–640)	568 (477–680)	413 (338–497)	<0.001
Race; <i>n</i> (%)				
White	165 (76.4)	101 (72.7)	64 (83.1)	0.02
Black	26 (12.0)	23 (16.6)	3 (3.9)	
Other	25 (11.6)	15 (10.8)	10 (13.0)	
Concurrent viral hepatitis				
None	147 (68.1)	80 (57.6)	67 (87.0)	<0.001
HBV	14 (6.5)	12 (8.6)	2 (2.6)	
HCV	44 (20.4)	36 (25.9)	8 (10.4)	
Both HBV and HCV	11 (5.1)	11 (7.9)	0 (0)	
Alcohol consumption				
None/occasional	169 (78.2)	95 (68.4)	74 (96.1)	<0.001
Present alcohol abuse issues	15 (6.9)	14 (10.1)	1 (1.3)	
Past alcohol abuse issues	32 (14.8)	30 (21.6)	2 (2.6)	
Pack years of smoking; median (IQR)	0 (0–20)	0 (0–20)	0 (0–0)	0.32
ECOG status ^{<i>b</i>}				
0	135 (65.2)	90 (67.2)	45 (61.6)	0.11
1	58 (28.0)	38 (28.4)	20 (27.4)	
2	8 (3.9)	5 (3.7)	3 (4.1)	
3	6 (2.9)	1 (0.8)	5 (6.9)	
Child Pugh class				
1	168 (77.8)	102 (73.4)	66 (85.7)	0.90
2	46 (21.3)	35 (35.2)	11 (14.3)	
3	2 (0.9)	2 (1.4)	0	
MELD score; median (IQR)	7 (6–9)	8 (7–10)	6 (6–7)	0.17
Any comorbidity, <i>n</i> (%)	159 (73.6)	108 (77.7)	51 (66.2)	0.08

^{*a*} *P* value for comparison between men and women^{*b*} ECOG status was missing for nine patients

Table 2

Tumor and treatment characteristics of patients who underwent IAT for hepatic malignancies

	All patients (<i>n</i> = 216)	Men (<i>n</i> = 139)	Women (<i>n</i> = 77)	<i>P</i> value ^a
Indication for IAT; <i>n</i> (%)				
HCC	109 (50.5)	88 (63.3)	21 (27.2)	<0.001
ICC	28 (13.0)	9 (6.5)	19 (24.7)	
CRLM	14 (6.5)	9 (6.5)	5 (6.5)	
Metastases from NELM primary	35 (16.2)	20 (14.4)	15 (19.5)	
Metastases from other primary	30 (13.9)	13 (9.4)	17 (22.1)	
Location of liver lesion(s); <i>n</i> (%)				
Right lobe only	65 (30.1)	49 (35.3)	16 (20.8)	0.02
Left lobe only	28 (13.0)	13 (9.4)	15 (19.5)	
Bilobar	123 (56.9)	77 (55.4)	46 (59.7)	
Grade of tumor; <i>n</i> (%)				
Well differentiated	34 (43.6)	21 (46.7)	13 (39.4)	0.03
Moderately differentiated	23 (29.5)	13 (28.9)	10 (30.3)	
Poorly differentiated	21 (26.9)	11 (24.4)	10 (30.3)	
Not available	138	94	44	
Number of lesions				
1	57 (26.4)	38 (27.3)	19 (24.7)	0.04
2–5	46 (21.3)	36 (25.9)	10 (13.0)	
6	113 (52.3)	65 (46.8)	48 (62.3)	
Size largest lesion (cm); median (IQR)	5.8 (3.7–9.4)	5.7 (3.6–9.3)	5.8 (3.7–9.5)	0.64
Previous liver directed surgery; <i>n</i> (%)	29 (13.4)	15 (10.8)	14 (18.2)	0.13
Previous systemic chemotherapy; <i>n</i> (%)	62 (28.7)	34 (25.2)	27 (35.1)	0.12
Number of IAT sessions; median (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	0.82
Intent of IAT				
Symptom control	167 (77.3)	108 (77.7)	59 (76.6)	0.43
Enhance potential tumor resectability	42 (19.4)	25 (18.0)	17 (22.1)	
Bridge to OLT	7 (3.2)	6 (4.3)	1 (1.3)	

^a*P* value for comparison between men and women

Table 3

Sarcopenia and hospital stay, morbidity, and mortality among men and women

	Men			Women		
	Sarcopenia (<i>n</i> = 36)	No sarcopenia (<i>n</i> = 103)	<i>P</i> value	Sarcopenia (<i>n</i> = 19)	No sarcopenia (<i>n</i> = 58)	<i>P</i> value
Hospital stay for >1 day; <i>n</i> (%)	4 (11.1)	9 (8.7)	0.74	3 (15.8)	12 (20.7)	0.72
ICU admission; <i>n</i> (%)	0	1 (1.0)	1.00	0	0	
Post-IAT morbidity						
Any complication; <i>n</i> (%)	4 (11.1)	5 (4.9)	0.24	0	8 (13.8)	0.19
Clavien grade 3 complication; <i>n</i> (%)	0	1 (1.0)	1.00	0	2 (3.5)	1.00
Post-IAT mortality						
30 days; <i>n</i> (%)	0	1 (1.0)	1.00	0	3 (5.2)	0.58
90 days; <i>n</i> (%)	6 (16.7)	9 (8.7)	0.19	1 (5.3)	6 (10.3)	0.67
1 year; <i>n</i> (%)	14 (38.9)	27 (26.2)	0.15	5 (26.3)	17 (29.3)	0.80
3 years; <i>n</i> (%)	18 (50.0)	33 (32.0)	0.05	8 (42.1)	24 (41.4)	0.96
5 years; <i>n</i> (%)	20 (55.6)	34 (33.0)	0.02	8 (42.1)	25 (43.1)	0.93
Survival (months); median (95 % CI)	17.0 (9.2–11.1)	33.3 (19.4–77.5)	0.02	15.8 (9.2–70.2)	22.1 (14.1–96.0)	0.81

Table 4

Cox proportional hazard ratio estimates for the effect of sarcopenia on mortality after adjustment for other covariates (lowest vs. highest quartile)

	Univariate		Multivariate	
	Hazard ratio (95 % CI)	P value	Hazard ratio (95 % CI)	P value
Sarcopenia (lowest vs. highest quartile)	2.20 (1.15–4.30)	0.02	1.84 (1.03–3.64)	0.04
Age at surgery (years)	1.00 (0.99–1.02)	0.76	–	
Weight (kg)	1.00 (0.99–1.01)	0.74	–	
Male gender	1.22 (0.78–1.92)	0.38	–	
White race	2.13 (0.90–5.09)	0.08	1.68 (0.69–4.10)	0.25
Largest tumor ≤ 5 cm	1.84 (1.18–2.86)	0.01	2.29 (1.13–4.62)	0.02
>1 tumor	1.61 (0.97–2.66)	0.07	3.28 (1.35–7.97)	0.01
Primary liver cancer	1.26 (0.81–1.98)	0.31	–	
Child class >1	2.15 (1.34–3.43)	<0.001	4.10 (1.95–8.65)	<0.001
IAT sessions >1	3.40 (2.11–5.48)	<0.001	4.67 (1.95–8.65)	<0.001
Systemic chemotherapy	0.91 (0.57–1.47)	0.70	–	
Clavien–Dindo grade ≥ 3 complications	5.14 (0.69–38.10)	0.11	–	