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Sarcopenia Adversely Impacts Postoperative Complications Following Resection or Transplantation in Patients with Primary Liver Tumors

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Abstract

Background—Sarcopenia is a surrogate marker of patient frailty that estimates the physiologic reserve of an individual patient. We sought to investigate the impact of sarcopenia on short- and long-term outcomes in patients having undergone surgical intervention for primary hepatic malignancies.

Methods—Ninety-six patients who underwent hepatic resection or liver transplantation for HCC or ICC at the John Hopkins Hospital between 2000 and 2013 met inclusion criteria. Sarcopenia was assessed by the measurement of total psoas major volume (TPV) and total psoas area (TPA). The impact of sarcopenia on perioperative complications and survival was assessed.

Results—Mean age was 61.9 years and most patients were men (61.4 %). Mean adjusted TPV was lower in women (23.3 cm³/m) versus men (34.9 cm³/m) ($P<0.01$); 47 patients (48.9 %) had sarcopenia. The incidence of a postoperative complication was 40.4 % among patients with sarcopenia versus 18.4 % among patients who did not have sarcopenia ($P=0.01$). Of note, all Clavien grade 3 complications ($n=11$, 23.4 %) occurred in the sarcopenic group. On multivariable analysis, the presence of sarcopenia was an independent predictive factor of postoperative complications (OR=3.06). Sarcopenia was not associated with long-term survival (HR=1.23; $P=0.51$).

Conclusions—Sarcopenia, as assessed by TPV, was an independent factor predictive of postoperative complications following surgical intervention for primary hepatic malignancies.

Keywords

Sarcopenia; Liver cancer; Hepatocellular carcinoma; Intrahepatic cholangiocarcinoma; Outcomes; Liver surgery

Introduction

Hepatocellular carcinoma (HCC) and intrahepatic cholangio-carcinoma (ICC) are the two most common primary liver tumors with 33,190 new cases expected to be diagnosed in 2014 and an incidence that has steadily risen by 4.1 % each year over the last decade.¹ Surgical resection or transplantation continues to offer the best chance for cure in patients with localized hepatic malignancies as systemic agents have limited efficacy.^{2–7} Prior to surgical intervention, the surgeon must estimate whether a patient possesses the physiologic reserve to tolerate a major surgical procedure. Patient variables such as age and preexisting medical comorbidities may help to estimate the risk associated with an operative intervention for a particular patient. The decision to operate remains, however, largely subjective and often

depends on an individual surgeon's experience—thus leading to significant variability in patient selection.^{8, 9}

Patient performance status (PS) has been demonstrated to predict treatment response and long-term survival in cancer patients.^{10–12} Despite its prognostic value, the available methods to gauge PS rely on qualitative models such as the Karnofsky, Eastern Cooperative Oncology Group (ECOG), and the Lansky performance scoring systems.^{13–16} As such, more objective measurements of physiologic reserve are needed to augment PS scoring models. Frailty, defined as the biologic syndrome that places a patient at increased vulnerability to adverse outcomes following a physiologically stressful event, is a more objective measure of physiologic reserve.¹⁷ While all surgical procedures may induce a stress state, hepatic resection and liver transplantation have the potential to result in more stress and therefore an increased risk of perioperative morbidity and mortality relative to other general surgery operations.^{18–23} In turn, the preoperative identification of patients at high risk of experiencing perioperative complications is important to allow for preoperative patient selection, as well as “pre-habilitation” conditioning in the hopes of optimizing outcomes following surgical intervention.^{24–26}

Sarcopenia, defined as the chronic loss of whole body muscle mass, is one such measure of frailty. Our group and others have validated sarcopenia as a predictor of morbidity and mortality in several patient populations, including patients undergoing surgery for pancreas cancer and colorectal liver metastasis.^{18–23} Sarcopenia has implicit appeal as a tool to assess preoperative frailty because the measurement of sarcopenia is relatively simple, and the metric is quantitative and objective. We sought to determine the impact of sarcopenia on outcomes following resection or transplantation of patients with primary liver tumors. Specifically, the objective of the current study was to define the incidence of sarcopenia and characterizes the effect of sarcopenia on both short- and long-term morbidity and mortality among patients undergoing surgery for HCC or ICC. In addition, while most previous studies have exclusively utilized only total psoas area (TPA) to assess sarcopenia, we examined the relative accuracy of total psoas volume (TPV) to define sarcopenia and predict outcomes.^{18, 19, 21, 27, 28}

Methods

Patients and Data Collection

Between 2000 and 2013, 328 patients who underwent hepatic resection with curative intent or orthotopic liver transplantation (OLT) for HCC or ICC were identified from the Johns Hopkins Hospital liver database; only patients with well-compensated liver function (Child-Pugh A) were included. Perioperative abdominal CT images (i.e., within 60 days before surgery or 10 days after surgery) were available for re-review for 96 patients, representing the study cohort. Clinicopathologic data includes information on demographics, hepatitis status (HBV and HCV), tumor characteristics (size, number, grade, stage, etc.), operative details, and length of hospital stay (LOS). Data on perioperative morbidity and mortality, as well as long-term overall disease-free survival, were also collected. Complications were scored by Clavien–Dindo classification with major complications being defined as Clavien

grade 3.²⁹ Appropriate approval was obtained from the Johns Hopkins Institutional Review Board.

Image Analysis

To assess sarcopenia, cross-sectional imaging of the abdomen (venous phase) was reviewed to determine the size of the psoas major muscle. The psoas was measured at the level of L3 on the first slice where both iliac crests were visible.¹⁹ 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 (HUs) to exclude vasculature and areas of fatty infiltration from the volumetric calculations. As previously described, TPA was assessed by measuring the two-dimensional cross-sectional area of the right and left psoas muscles at the level of L3.¹⁹ In contrast, TPV was measured using AW Workstation Volume Viewer Software (GE Healthcare, Little Chalfont, UK) by hand tracing the borders of the entire psoas muscle. We performed three manual measurements of the psoas major muscle skipping four slices between measurements equating to a total psoas length of 55 cm for all volume measurements (Fig. 1). TPA was quantified using ImageJ (National Institutes of Health, Bethesda, Maryland, USA).³⁰ Both TPV and TPA were normalized for height. Two trained observers performed all measurements (N.A. and V.V.). Concordance between measurements was examined by pairwise correlations, which exhibited an interobserver agreement of 97.0 %.

Statistical Analysis

Data were reported as mean and standard deviation (SD) for continuous variables. The impact of sarcopenia was evaluated as both a continuous and categorical variable. As previously reported and validated, we used log-rank χ^2 statistic analysis to perform sensitivity analysis to define sex specific cut-off values for sarcopenia.²⁷ The TPA cut-off to define sarcopenia was 642.1 and 784.0 mm²/m² for women and men, respectively; the cutoff for TPV was 22.93 cm³/m for women and 34.14 cm³/m for men.^{22, 27} Given that preliminary analyses revealed that baseline muscle mass (both TPA and TPV) was comparable among patients undergoing transplantation or resection, these patients were combined into a single analytic cohort (Supplemental Table). The impact of sarcopenia on morbidity and mortality was examined using univariable and multivariable logistic regression analyses. Overall and disease-free survival were analyzed by the non-parametric Kaplan–Meier method. To identify prognostic factors after surgical intervention, variables significant on univariable analysis, as well as those factors of clinical significance, were included in the overall multivariable Cox proportional hazards model OS. We used receiver-operating characteristics (ROC) to compare the predictive powers of TPA versus TPV. A *P* value of <0.05 was considered statistically significant. The statistical software package, Stata 12.0 (Stata Corp, College Station, TX, USA) was used for all analyses.

Results

Demographics and Clinical Characteristics

Ninety-six unique patients met inclusion criteria for the study and their clinicopathologic characteristics are outlined in Table 1. Mean age was 61.9 years and there were 59 (61.4 %)

men and 37 (38.6 %) women in the study population. HCC served as the primary indication for operative intervention with 69.8 % of patients having HCC versus 30.2 % of patients having ICC. At the time of surgery, the operative procedure consisted of wedge resection (21.9 %), major hepatectomy (42.7 %), extended hepatectomy (13.5 %), and transplant (21.9 %). Mean tumor size was 5.7 cm and most patients (69.2 %) had a solitary lesion. All patients who underwent transplantation had HCC, while patients with ICC were treated exclusively with hepatic resection. Patients who underwent transplantation were younger, more likely to have hepatitis, and end-stage liver disease/cirrhosis ($P<0.05$). In contrast, other clinical attributes such as BMI, number of hepatic lesions, albumin level, and tumor stage were comparable between transplant and non-transplant patients (Supplemental Table).

The average TPA was $784.4 \text{ mm}^2/\text{m}^2$ after normalizing for patient height. When stratified by gender, the mean adjusted TPA was lower for women than for men (638.9 vs. $818.2 \text{ mm}^2/\text{m}^2$, $P<0.001$) (Fig. 2a). The lowest quartile TPA threshold for men was 680.4 versus $524.7 \text{ mm}^2/\text{m}^2$ 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). Of note, TPA was comparable in transplant ($754.1 \text{ mm}^2/\text{m}^2$) and resection ($726.8 \text{ mm}^2/\text{m}^2$) patients ($P=0.57$). Sarcopenia was noted across a wide range of BMIs. Sarcopenia was less frequently observed, however, among obese patients with a BMI $30 \text{ kg}/\text{m}^2$. Of the 23 patients who had a BMI $30 \text{ kg}/\text{m}^2$, 5 (21.7 %) also had sarcopenia based on TPA and therefore were characterized as having sarcopenic obesity. In contrast, among patients with a BMI $24.9 \text{ kg}/\text{m}^2$, the incidence of sarcopenia was 64.7 %.

While TPA has traditionally been the most commonly reported method to assess sarcopenia, with the introduction and adoption of three-dimensional imaging, there has been increasing interest in morphometric volumetric analyses. As such, we sought to assess sarcopenia separately using TPV. The mean TPV was $30.4 \text{ m}^3/\text{m}$ after normalizing for patient height. Similar to TPA, the mean adjusted TPV was lower among women than among men (23.3 vs. $34.9 \text{ cm}^3/\text{m}$, respectively; $P<0.01$) (Fig. 3a). Sarcopenia based on TPV was also noted to increase with age (Fig. 3b); TPV was comparable in transplant ($29.5 \text{ cm}^3/\text{m}$) versus resection ($30.7 \text{ cm}^3/\text{m}$) patients ($P=0.54$). In total, 44 (45.8 %) patients had sarcopenia defined by TPA versus 47 patients (48.9 %) using TPV.

Among patients who had sarcopenia defined by TPV, the incidence of a postoperative complication was 40.4 % compared with 18.4 % for patients who did not have sarcopenia. ROC analysis was performed to evaluate the accuracy of TPA versus TPV to predict postoperative complications. TPV tended to have a modest increased ability to predict morbidity following surgery for primary liver malignancies (TPV, $\text{AUC}=0.63$; TPA, $\text{AUC}=0.57$; $P=0.12$). Because TPV tended to be a more accurate assessment of sarcopenia, all subsequent analyses were performed using TPV.

Impact of Sarcopenia on Short-Term Outcomes

Of the 96 patients who underwent transplantation or resection, 28 experienced at least one complication for an overall morbidity of 29.1 % (transplantation, 33.3 % vs. resection, 26.7 %; $P=0.31$). Morbidity after surgery included biloma ($n=6$), surgical site infection ($n=4$),

liver insufficiency ($n=4$), sepsis ($n=4$), pneumonia ($n=4$), renal failure ($n=4$), cardiac arrest ($n=1$), and postoperative hemorrhage ($n=1$). The incidence of a postoperative complication was 40.4 % among patients with sarcopenia versus 18.4 % among patients who did not have sarcopenia ($P=0.01$). In fact, patients who had sarcopenia had a threefold higher risk of a postoperative complication compared with patients who did not have sarcopenia ($OR=3.01$, 95 % $CI=1.19-7.63$; $P=0.02$). In addition, all major complications that occurred in postoperative period were among patients with sarcopenia; specifically, the 11 (23.4 %) patients who experienced a Clavien grade 3 complication had sarcopenia. In multivariable analyses, after accounting for other competing risks including type of operative procedure (i.e., transplantation vs. resection), sarcopenia remained independently associated with a higher risk of postoperative morbidity ($OR=3.06$, 95 % $CI=1.07-8.72$; $P=0.03$) (Table 2).

Mean hospital stay for the entire cohort was 12.1 days and did not differ among patients with or without sarcopenia ($P=0.50$) (Table 3). There were five deaths within 90 days, for a periprocedural mortality of 5.2 % (no sarcopenia, $n=1$ vs. sarcopenia, $n=4$; $P=0.20$).

Impact of Sarcopenia on Survival

For the entire cohort, median overall survival was 53.3 months, whereas overall 1-, 3-, and 5-year survival were 81.8, 56.8, and 46.8 %, respectively. Mortality rates of sarcopenic versus non-sarcopenic patients are compared in Table 3. On univariable analysis, several factors were associated with worse overall survival including vascular invasion ($HR=3.23$, 95 % $CI=1.71-6.43$; $P<0.01$), poorly differentiated tumor grade ($HR=6.47$, 95 % $CI=1.84-22.72$; $P<0.01$), and tumor size ($HR=2.06$, 95 % $CI=1.07-3.98$; $P=0.03$) (Table 4). Sarcopenia was not associated with overall survival ($HR=1.23$, 95 % $CI=0.65-2.34$; $P=0.51$). The 5-year overall (no sarcopenia, 52.5 % vs. sarcopenia, 41.8 %) and disease-free (no sarcopenia, 50.1 % vs. sarcopenia, 37.8 %) were not impacted by the presence or absence of sarcopenia (both $P>0.05$) (Fig. 4).

Discussion

Hepatic resection and transplantation play a central role in the management of patients with HCC and ICC tumors. While the perioperative mortality associated with these surgical procedures has dramatically decreased over the last several decades,^{3, 31} perioperative morbidity continues to be as high as 45 % in some studies.^{2, 3, 31-33} The occurrence of a perioperative complication cannot only adversely impact patient quality-of-life and increase health-care resource utilization, but also be detrimental to long-term oncological outcomes.³⁴ Identification of patients at greatest risk of perioperative complications remains a challenge. While patient age is not necessarily associated with outcomes following hepatic surgery, patient-level physiological/performance status is important.³⁵ In fact, frailty, which is a global metric of patient physiological reserve and overall health status, strongly correlates with patient outcome following a number of procedures.³⁶ Frailty, however, can be difficult to assess, as well as non-reproducible and subject to measurement or reporting bias.^{11,18, 19, 37} Our group, and others, have previously reported on the use of TPA to determine sarcopenia and, in turn, have utilized sarcopenia to stratify patients with regard to perioperative outcomes.^{18, 19, 21, 22, 28, 38} In the current study, we noted that sarcopenia was

a determinant of short-term morbidity following hepatic resection or transplantation for HCC and ICC. Of note, we found that patients who had sarcopenia had a threefold increased risk of a postoperative complication. In addition, all patients who had a major complication had underlying sarcopenia. Unlike previous studies, we assessed sarcopenia using both cross-sectional (TPA) and volumetric (TPV) analyses, which allowed for a more complete assessment of psoas muscle mass. Compared with TPA, TPV tended to have a modest increased ability to predict morbidity following surgery for primary liver malignancies.

Unlike cachexia, which is typically associated with weight loss due to chemotherapy or a general malignancy-related cachexia syndrome, sarcopenia relates to muscle mass rather than simply weight. Muscle loss and adipose accumulation within the psoas that are observed in patients with sarcopenia is a characteristic of global muscle wasting induced by physiologic age, underlying comorbidities, and disease-related stresses. As such, while weight reflects nutritional status, sarcopenia—the loss of muscle mass—is a more accurate and quantitative global marker of frailty.^{18, 19, 21, 39} Several investigators have noted that patients with sarcopenia who are treated with chemotherapy have worse outcomes compared with non-sarcopenic patients.^{40–42} Sarcopenia has also been noted to impact outcomes following certain operative approaches.^{18–20, 22, 38} Our group had previously reported that sarcopenia negatively impacted short-term outcomes among patients undergoing hepatic resection for colorectal liver metastasis.²² Similarly, in the current study, we noted that sarcopenia conferred a significant increased risk of a postoperative complication. In fact, patients with sarcopenia had a threefold increased risk of having any postoperative complication. Of note, every patient who experienced a major complication (Clavien grade 3) had sarcopenia. Given the importance of risk stratification, sarcopenia may be an important preoperative factor to help providers and patients make informed decisions concerning the risks of surgery.

While sarcopenia has an adverse impact on short-term perioperative outcomes, its influence on long-term survival and mortality is less defined. Our group had previously reported that sarcopenia was associated with a worse long-term survival among patients undergoing surgical resection of pancreatic adenocarcinoma, but not patients following hepatic resection of colorectal metastasis.^{22, 28} For patients with hepatic malignancies, sarcopenia had similarly been shown to be associated with survival following intra-arterial therapy and surgery. Specifically, we previously reported that sarcopenia was an independent predictor of mortality following intra-arterial therapy with sarcopenic patients having a twofold increased risk of death.¹⁹ Similarly, Englesbe et al. and Harimoto et al. reported a worse survival among sarcopenic patients following liver transplantation and resection, respectively.^{18, 21} In the current study, we did not find a difference in long-term outcome among patients with and without sarcopenia. The reason for this is undoubtedly multifactorial. While the previous studies focused exclusively on HCC, our study included both HCC and ICC and previous data have suggested that the impact of sarcopenia may vary based on diagnosis. In addition, while previous studies included either transplantation or resection exclusively, the current study cohort included patients who underwent either procedure. Finally, the effect of sarcopenia on survival may be more understated and not as powerful factor driving long-term outcomes as other biological factors such as tumor size, grade, and the presence of vascular invasion. As such, our study may have been

underpowered to detect any effect of sarcopenia on survival; a larger sample size may be necessary to identify a difference in survival among patients with and without sarcopenia.

With post-processing tools, efficient and reliable three-dimensional assessment and volumetric measurements have become possible. These techniques have been successfully applied to assess the volume of the liver, as well as assess response after therapy.^{43–47} Volumetric analyses have also been shown to be reproducible and have minimal interobserver variability.^{43, 48–50} In addition, volumetric analysis can be performed in a semi-automated manner to allow for more methodical assessment. Perhaps, most importantly, volumetric analysis allows for a more complete assessment of the total tissue in question compared with the much more limited cross-sectional assessment used to estimate area (Fig. 1). Using AW Workstation Volume Viewer Software (GE Healthcare, Little Chalfont, UK), we were able to measure slightly more than half the volume of the psoas major muscle (55 cm). To our knowledge, the current study was the first to use volumetric measurements to assess the psoas and define sarcopenia. Using TPV to define sarcopenia, we found that TPV tended to have an increased ability to predict morbidity following surgery for primary liver malignancies (TPV, AUC=0.63 vs. TPA, AUC=0.57; $P=0.12$). Future studies should continue to assess the role of assessing TPV rather than TPA to define sarcopenia as a possible means to increase the sensitivity of predicting perioperative morbidity.

There are several limitations that need to be considered when interpreting the data. For the purposes of analyses, we combined patients who had undergone either transplantation or resection. While we believe the combination was justified because the groups had comparable baseline muscle mass parameters as well as overall postoperative morbidity, there may be differences in how sarcopenia impacts the outcome of patients undergoing transplantation versus resection that we failed to detect. In addition, due to the retrospective nature of the study, we were unable to collect data on other measures of frailty such as walking speed and handgrip strength. While there were more patients who had undergone either transplantation or resection for HCC or ICC, only a smaller subset had cross-sectional imaging performed at Johns Hopkins and was available for re-review. In turn, as noted, the sample size was somewhat limited ($n<100$) and may have affected our ability to detect more subtle statistical differences between the sarcopenia and no sarcopenia groups. Specifically, the effect of sarcopenia on survival is not well defined. While some studies have noted an association between sarcopenia and long-term survival,^{18, 19, 28} other data²² have failed to note the impact of sarcopenia on survival. The effect of sarcopenia on short-term perioperative outcomes is more established and this is the reason why sarcopenia has been proposed as a perioperative tool to assess frailty.²⁰ The data in the current study confirm that sarcopenia is associated with risk of perioperative morbidity; however, its association with mortality warrants future study.

In conclusion, perioperative morbidity following transplantation and resection of HCC and ICC occurred in nearly one in three patients. Patients who had sarcopenia were at a threefold increased risk of a complication and all major complications occurred among patients with sarcopenia. Sarcopenia appears to be an objective measure of frailty that can be used to stratify patients with regard to risk of postoperative complications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Sarcopenia measurement using total psoas area and volume. **a** Axial CT image of the abdomen obtained in the portal venous phase. Hand tracing of the psoas major muscle was performed (*arrows*) to determine area of the psoas muscles at the level of the iliac crest. **b** Coronal 3D image of the abdomen in shaded surface display showing the entire volume of the psoas muscle bilaterally (*arrows*). Total psoas muscle volume on the right and left is 250 and 269 cm³, respectively

Fig. 2.

Comparison of sarcopenia distribution across gender and age as measured by total psoas area (TPA). **a** Distribution of TPA (mm^2/m^2) stratified by gender. **b** Distribution of TPA (mm^2/m^2) by age

Fig. 3. Comparison of sarcopenia distribution across gender and age as measured by total psoas volume (TPV). **a** Distribution of TPV (cm^3/m) according to gender. **b** Distribution of TPV (cm^3/m) according to age

Fig. 4. Sarcopenia does not impact survival in primary hepatic malignancies. Kaplan–Meier survival analysis as stratified by the presence of sarcopenia based on total psoas volume. Both **a** overall survival and **b** disease-free survival are not impacted by the presence of sarcopenia

Table 1

Demographics and clinical characteristics of patients who underwent curative intent surgery for primary hepatic malignancies

	All patients (n=96)	Men (n=59)	Women (n=37)	P value *
Age at surgery (years)	61.9±12.3	63.5±10.3	59.3±14.9	0.19
BMI (kg/m ²)	27.4±5.4	27.3±4.8	27.5±6.4	0.80
Total psoas volume (cm ³ /m)	30.4±8.9	34.9±7.4	23.3±5.9	<0.001
Total psoas area (mm ² /m ²)	784.4±189.9	818.2±179.01	638.9±152.74	<0.001
Race				
White	72 (75.0 %)	43 (72.9 %)	29 (78.4 %)	0.58
Black	12 (12.5 %)	7 (11.9 %)	5 (13.5 %)	
Other	12 (12.5 %)	9 (15.2 %)	3 (8.1 %)	
Current viral hepatitis				
None	56 (58.3 %)	28 (47.4 %)	28 (75.7 %)	0.04
HBV	10 (10.4 %)	21 (35.6 %)	7 (18.9 %)	
HCV	28 (29.2 %)	8 (13.6 %)	2 (5.4 %)	
Both HBV and HCV	2 (2.1 %)	2 (3.4 %)	–	
Diabetes	22 (23.4 %)	17 (29.3 %)	5 (13.9 %)	0.08
Cirrhosis	34 (35.4 %)	25 (42.3 %)	9 (24.3 %)	
MELD score	10.2±5.7	10.4±5.8	9.7±5.7	0.28
Albumin (g/dL)	3.7±0.8	3.7±0.7	3.7±0.8	0.54
Alcohol consumption	33 (34.7 %)	27 (46.5 %)	6 (16.2 %)	<0.001
Tobacco smoking	44 (50.6 %)	33 (61.1 %)	11 (33.3 %)	0.001
Indication for surgery				
End-stage liver disease	7 (7.3 %)	3 (5.1 %)	4 (10.8 %)	0.28
Malignancy	79 (82.3 %)	48 (81.3 %)	31 (83.8 %)	
Both	10 (10.4 %)	8 (13.6 %)	2 (5.4 %)	
Histopathological type				
HCC	67 (69.8 %)	46 (78.0 %)	21 (56.8 %)	0.03
ICC	29 (30.2 %)	13 (22.0 %)	16 (43.2 %)	
Location of tumor				
Right lobe only	43 (51.2 %)	29 (54.7 %)	14 (45.1 %)	0.64
Left lobe only	25 (29.8 %)	14 (26.4 %)	11 (35.5 %)	
Bilobar	16 (19.0 %)	10 (18.9 %)	6 (19.4 %)	
Grade of tumor				
Well differentiated	21 (21.9 %)	13 (22.0 %)	8 (21.6 %)	0.60
Moderately differentiated	51 (53.1 %)	30 (50.8 %)	21 (56.8 %)	
Poorly differentiated	21 (21.9 %)	15 (25.4 %)	6 (16.2 %)	
Not available	3 (3.1 %)	1 (1.7 %)	2 (5.4 %)	
Number of lesions				
Solitary	63 (69.2 %)	35 (62.5 %)	28 (80.0 %)	0.07
Multiple	28 (30.8 %)	21 (37.5 %)	7 (20.0 %)	

	All patients (n=96)	Men (n=59)	Women (n=37)	P value *
Size of largest lesion (cm)	5.7±4.6	4.9±3.4	6.9±5.9	0.07
T category				
T1	42 (43.7 %)	24 (40.7 %)	18 (48.7 %)	0.79
T2	34 (35.4 %)	23 (39.0 %)	11 (29.7 %)	
T3	9 (9.3 %)	5 (8.5 %)	4 (10.8 %)	
Tx	11 (11.4 %)	7 (11.9 %)	4 (10.8 %)	
Nodal status				
N0	41 (42.7 %)	34 (57.6 %)	14 (37.8 %)	0.13
N1	7 (7.2 %)	22 (37.3 %)	19 (51.3 %)	
Nx	48 (50 %)	3 (5.1 %)	4 (10.8 %)	
Perivascular invasion	42 (44.2 %)	26 (44.1 %)	16 (44.4 %)	0.97
Type of surgery				
Wedge resection	21 (21.9 %)	15 (25.4 %)	6 (16.2 %)	
Major hepatectomy	41 (42.7 %)	24 (40.7 %)	17 (45.9 %)	
Extended hepatectomy	13 (13.5 %)	7 (11.9 %)	6 (16.2 %)	
Transplant	21 (21.9 %)	13 (22.0 %)	8 (21.6 %)	

Categorical data presented as number (percentage). Continuous data presented as mean±standard deviation

Mann–Whitney two-sample statistic for continuous data

BMI indicates body mass index, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *HCC* hepatocellular carcinoma, *ICC* intrahepatic cholangiocarcinoma, *T* tumor, *N* nodal

* *P* value comparing cohorts based on chi-square for categorical data

Table 2

Logistic regression on the correlation between postoperative complication and sarcopenia

	Univariable			Multivariable		
	OR	95 % CI		OR	95 % CI	P value
Age						
<60	Reference			Reference		
>60	1.33	0.53–3.32	0.53	1.69	0.49–5.88	0.40
Gender						
Women	Reference			Reference		
Men	3.07	1.10–8.52	0.03	3.98	1.28–12.39	0.01
Type of surgery						
Wedge resection	Reference			Reference		
Major hepatectomy	1.37	0.37–5.03	0.63	2.53	0.59–10.72	0.20
Extended Hepatic resection	3.64	0.78–17.01	0.10	6.80	1.13–40.77	0.03
Transplant	2.61	0.64–10.61	0.17	7.64	0.66–87.48	0.10
MELD score	1.07	0.99–1.16	0.10	1.07	0.95–1.20	0.28
Albumin (g/dL)	0.55	0.30–0.99	0.04	0.44	0.16–1.21	0.11
BMI (kg/m ²)	0.93	0.84–1.02	0.11	0.94	0.82–1.07	0.32
Sarcopenia						
Absence	Reference			Reference		
Presence	3.01	1.19–7.63	0.02	3.06	1.07–8.72	0.03

Table 3

Comparison of hospital stay and mortality between sarcopenia and non-sarcopenia patients

	Sarcopenia (n=47)	No sarcopenia (n=49)	P value
Length of stay	12.1±13.1	9.7±11.1	0.50
Postoperative mortality			
30 days	2 (4.3 %)	0	0.24
90 days	4 (8.5 %)	1 (2.0 %)	0.20
1 year	11 (23.4 %)	6 (12.2 %)	0.15
3 year	18 (38.3 %)	14 (28.6 %)	0.31
5 year	21 (44.7 %)	15 (30.6 %)	0.16
Survival (month); median	38.5	69.1	0.32

Table 4

Cox proportional hazard ratio estimates for the effect of sarcopenia on mortality after adjustment for other covariates

	Univariable		Multivariable	
	Hazard ratio (95 % CI)	P value	Hazard ratio (95 % CI)	P value
Sarcopenia	1.23 (0.65–2.34)	0.51	1.34 (0.61–2.76)	0.43
Age at surgery (years)	1.00 (0.97–1.03)	0.59	–	
BMI (kg/m ²)	0.95 (0.89–1.01)	0.13	0.96 (0.90–1.03)	0.32
Male gender	1.15 (0.58–2.29)	0.67	–	
Largest tumor >5 cm	2.06 (1.07–3.98)	0.03	1.48 (0.71–3.08)	0.29
Poorly differentiated tumor	6.47 (1.84–22.72)	<0.01	2.74 (0.57–13.07)	0.20
Nodal metastasis	1.15 (0.33–43.99)	0.81	–	
Vascular invasion	3.23 (1.71–6.43)	<0.01	3.67 (1.61–8.3810.40)	0.002
Black versus white race	2.02 (0.94–4.32)	0.07	2.23 (0.89–5.53)	0.08
Other races versus white race	1.59 (0.65–3.87)	0.31	2.54 (0.91–7.09)	0.07
Multiple tumors	0.68 (0.33–1.43)	0.25	–	
Cirrhosis	1.34 (0.62–2.27)	0.59	–	

BMI body mass index