

Sarcopenia, but not visceral fat amount, is a risk factor of postoperative complications after major hepatectomy

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Received: 12 May 2015 / Accepted: 17 August 2015 / Published online: 4 September 2015
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Abstract

Background Major hepatectomy is associated with significant morbidity and mortality rates, particularly in patients aged more than 70 years. This study assessed whether physical indicators, such as sarcopenia and visceral fat amount, could predict morbidity and mortality after major hepatectomy.

Methods The study enrolled 144 patients who underwent curative major hepatectomy. Skeletal muscle and visceral fat amount at the third lumbar vertebra (L3) in the inferior direction were quantified using enhanced computed tomography scans. The patients were divided into two subgroups, with and without sarcopenia, based on median skeletal muscle mass in men and women (43.2 cm²/m² in men; 35.3 cm²/m² in women).

Results The study included 108 men and 36 women, with median skeletal muscle tissue of 43.2 and 35.3 cm²/m², respectively. The mortality rate was significantly higher in patients with than without sarcopenia [seven cases (9.7 %), one case (1.4 %), respectively; $P = 0.021$], whereas liver-related morbidity and mortality rates were similar. In patients aged >70 years, the morbidity, liver dysfunction-related morbidity, and mortality rates were significantly higher in patients with than without sarcopenia ($P < 0.05$

each). In contrast, surgical outcomes were similar in patients with high and low visceral fat amounts.

Conclusions Sarcopenia was a risk factor for postoperative complications after major hepatectomy, particularly in elderly patients.

Keywords Sarcopenia · Major hepatectomy · Complications

Introduction

Although advances in multimodal treatment options, such as radiofrequency ablation, interventional radiology, and chemotherapy, have improved survival rate in patients with liver cancer [1–3], hepatic resection still provides the best hope of cure [4]. Major hepatectomy, however, is still associated with significant morbidity (12.9–47.1 % [5–9]) and mortality (2.6–7.4 % [5–10]) rates, despite advances in surgical techniques and perioperative care. Postoperative complications lead to not only prolonged hospital stays but also greater medical costs, and, possibly, poorer long-term survival [11, 12]. Accurate assessments of future remnant liver function are crucial in avoiding or minimizing postoperative complications. However, some patients experience unexpected postoperative complications, despite a careful preoperative workup, suggesting that an alternative approach, considering not only liver function but general patient condition, is required to prevent morbidity after hepatectomy. Moreover, the number of elderly patients who undergo major hepatectomy is increasing, and this population is more likely to suffer from relevant disorders, such as cardiac or pulmonary dysfunction and diabetes mellitus, that may affect postoperative outcomes [13]. Indeed, the mortality rate following major hepatectomy was found to

Electronic supplementary material The online version of this article (doi:10.1007/s10147-015-0898-0) contains supplementary material, which is available to authorized users.

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be 11.1 % in patients aged more than 70 years compared with 3.6 % in younger patients [14].

Aging results in a progressive loss of muscle mass and strength, so-called sarcopenia. Sarcopenia may cause functional impairment, physical disability, and even mortality and has been associated with poorer long-term outcomes in cancer patients [15–20]. Sarcopenia has been reported to be a robust predictor of postoperative complications of general anesthesia [21, 22]. The prevalence of sarcopenia continues to increase worldwide and has been associated with the increase in the number of elderly persons.

Aging and physical disability have also been associated related with increases in fat mass, particularly visceral fat, which is important in the development of metabolic syndrome and other cardiovascular disease. Visceral fat amount has been reported to be associated with an increased incidence of many types of cancer [23]. Moreover, obesity itself has been reported to affect outcomes of abdominal surgery [24, 25].

The clinical significance of sarcopenia and visceral fat amount in surgical outcomes after hepatectomy remains unclear. We therefore analyzed whether sarcopenia or visceral fat amount could predict morbidity, liver-related morbidity, and overall mortality after major hepatectomy.

Patients and methods

Study subjects

A total of 144 consecutive patients who underwent major hepatectomy (three or more Couinaud's segments) at Kumamoto University Hospital (Kumamoto, Japan) between January 2007 and December 2013 were enrolled in this study. Patient characteristics are shown in Table 1. Of these patients, 44 (30.1 %) underwent preoperative portal vein embolization before major hepatectomy. Perioperative data were prospectively collected, and the association between objective factors of physical condition (such as sarcopenia and visceral fat amount) and surgical outcomes after major hepatectomy were retrospectively analyzed. Additionally, we also analyzed their impact in hepatocellular carcinoma (HCC) patients only. These patient characteristics are shown in Table S1.

Assessment of adipose and skeletal muscle tissue

All patients underwent preoperative multi-slice contrast-enhanced computed tomography (CT) (slice thickness, 2.5 mm). A transverse CT image of each scan at the third lumbar vertebra (L3) in the inferior direction was used to calculate the amounts of adipose and skeletal muscle tissues [20]. The areas of skeletal muscle mass and visceral

fat amount were measured by the Synapse Vincent system. Skeletal muscle was identified and quantified by Hounsfield unit (HU) thresholds of -29 to $+150$ (water is defined as 0 HU, air as 1000 HU). The areas of visceral fat were calculated by measuring pixels with densities in the range of -190 to -30 HU [26, 27]. Briefly, visceral fat amounts were quantified in several muscles, including the psoas, erector spine, quadratus lumborum, transversus abdominis, rectus abdominis, and external and internal oblique abdominal muscles (Fig. 1). The cross-sectional area of each segment was normalized by height (cm^2/m^2). Because sarcopenia criteria are different between Japanese and Western people, we divided the patients into two subgroups with and without sarcopenia based on the median skeletal muscle mass in men and women ($43.2 \text{ cm}^2/\text{m}^2$ in men and $35.3 \text{ cm}^2/\text{m}^2$ in women). Cutoff values for visceral fat amount were determined as 103 cm^2 for men and 69 cm^2 for women, which are recognized as measures of metabolic abnormalities in Japan [28].

Definition of surgical outcomes

The main surgical outcomes in the present study were morbidity, including liver-related morbidity, and mortality after major hepatectomy. Complications were categorized using the modified Clavien classification system [29, 30]. Morbidity (i.e., serious complications) was defined as grade III or greater (IV and V). Liver-related morbidity was defined as a serum bilirubin level $>3.0 \text{ mg/dl}$ ($50 \mu\text{mol/l}$) and/or a prothrombin time index $<50 \%$ of the normal value on or after postoperative day 5, along with clinical symptoms, such as refractory ascites, hepatic encephalopathy, and hepatorenal syndrome, requiring intensive care treatment and defined as grade C post-hepatectomy liver failure by the International Study Group of Liver Surgery [9, 31]. Mortality was defined as any death that occurred during the same hospital stay or within 3 months after major hepatectomy.

Statistical methods

Continuous variables are expressed as median (range) unless otherwise stated and compared using Student's *t* tests. We constructed a multivariate model to compute a hazard ratio (HR) according to morbidity, liver-related morbidity, and mortality. Cox model odds ratios (OR) with 95 % confidence intervals (CI) were calculated. $P < 0.05$ was considered statistically significant. All analyses were performed using JMP (Version 9; SAS Institute, Cary, NC, USA) software.

Table 1 Clinical and perioperative factors relative to sarcopenia and visceral fat amount in 144 patients

Clinical factors	All patients (<i>N</i> = 144) (%)		Sarcopenia		<i>P</i>	Visceral fat amount		<i>P</i>
	Present (<i>n</i> = 72) (%)	Absent (<i>n</i> = 72) (%)	Present (<i>n</i> = 72) (%)	Absent (<i>n</i> = 72) (%)		Low (<i>n</i> = 75) (%)	High (<i>n</i> = 69) (%)	
Age (years)	65.1 ± 10.1	64.9 ± 11.6	65.4 ± 8.4	65.4 ± 8.4	0.95	65 ± 10.4	65 ± 9.7	0.99
Sex (male/female)	108/36	54/18	54/18	54/18	1	55/20	53/16	0.55
Skeletal muscle mass (cm ² /m ²)	41.4 ± 7.8	36.1 ± 4.8	46.70 ± 6.5	46.70 ± 6.5	<0.001	39.0 ± 6.6	43.8 ± 7.3	<0.001
Body mass index (kg/m ²)	22.9 ± 4.2	21.6 ± 4.7	24.2 ± 3.2	24.2 ± 3.2	0.0012	21.3 ± 4.4	24.7 ± 3.2	<0.001
Visceral fat amount (cm ²)	89.5 ± 58.8	71.5 ± 50.7	103.5 ± 60.7	103.5 ± 60.7	0.001	44.7 ± 28	139.7 ± 40.5	<0.001
Albumin (g/dl)	4.0 ± 0.5	3.9 ± 0.5	4.0 ± 0.5	4.0 ± 0.5	0.74	3.9 ± 0.5	4.0 ± 0.6	0.23
Total bilirubin (mg/dl)	0.8 ± 0.3	0.8 ± 0.4	0.8 ± 0.3	0.8 ± 0.3	0.61	0.8 ± 0.3	0.8 ± 0.4	0.24
Platelet count (×10 ⁴ /μl)	21.1 ± 28.2	21.6 ± 24.1	20.6 ± 31.8	20.6 ± 31.8	0.53	17.7 ± 8.0	24.2 ± 39	0.17
ICGR ₁₅ (%)	12.7 ± 7.8	13.1 ± 8.2	12.3 ± 7.4	12.3 ± 7.4	0.84	12.7 ± 7.6	12.9 ± 8.0	0.93
Viral infection (HBV/HCV/nomB-nonC)	28/43/101	14/25/47	14/18/54	14/18/54	0.2	15/25/34	13/18/37	0.4
Preoperative therapy (present/absent)	49/95	29/43	20/52	20/52	0.07	27/48	22/47	0.52
Tumor size (cm)	6.4 ± 4.2	6.7 ± 4.5	6.2 ± 3.7	6.2 ± 3.7	0.59	7.1 ± 4.9	5.76 ± 3.3	0.1
Number of tumors	2.1 ± 1.7	2.2 ± 2.2	2.1 ± 1.3	2.1 ± 1.3	0.97	2.3 ± 2.1	1.9 ± 1.2	0.29
Transfusion	6 (4.1 %)	4 (5.6 %)	2 (2.8 %)	2 (2.8 %)	0.41	3 (0.04 %)	3 (4.3 %)	0.41
Operative time (min)	436 ± 95	423 ± 90	449 ± 98	449 ± 98	0.12	418.2 ± 93	451 ± 96	0.036
Blood loss (ml)	573 ± 1069	666 ± 1452	475 ± 333	475 ± 333	0.31	651 ± 1462	504 ± 342	0.442
Morbidity	43 (30 %)	23 (32 %)	20 (28 %)	20 (28 %)	0.58	25 (33 %)	18 (26 %)	0.5
Liver-related morbidity	11 (7.6 %)	8 (11 %)	3 (4.2 %)	3 (4.2 %)	0.11	6 (8 %)	5 (7.2 %)	0.9
Mortality	8 (5.6 %)	7 (9.7 %)	1 (1.4 %)	1 (1.4 %)	0.021	3 (4 %)	5 (7.2 %)	0.37
Diagnosis								
Hepatocellular carcinoma	91 (63 %)	45 (63 %)	46 (64 %)	46 (64 %)	0.91	47 (63 %)	44 (64 %)	0.94
Intrahepatic cholangiocarcinoma	18 (13 %)	9 (13 %)	9 (13 %)	9 (13 %)	1	11 (15 %)	7 (10 %)	0.64
Liver metastasis	23 (16 %)	13 (18 %)	10 (14 %)	10 (14 %)	0.87	12 (16 %)	12 (17 %)	0.92
Other	12 (8.3 %)	5 (6.9 %)	7 (9.7 %)	7 (9.7 %)	0.65	5 (7 %)	6 (8.7 %)	0.89
Operative methods								
Left hepatectomy	45 (31 %)	21 (29 %)	24 (33 %)	24 (33 %)	0.76	25 (34 %)	20 (28 %)	0.79
Left trisegmentectomy	5 (3.5 %)	2 (2.8 %)	3 (4.2 %)	3 (4.2 %)	0.53	2 (2.6 %)	3 (4.4 %)	0.53
Right hepatectomy	82 (57 %)	43 (60 %)	39 (54 %)	39 (54 %)	0.83	41 (54 %)	41 (60 %)	0.72
Right trisegmentectomy	6 (4.2 %)	3 (4.2 %)	3 (4.2 %)	3 (4.2 %)	1	4 (5.3 %)	2 (2.9 %)	0.43
Central bisegmentectomy	6 (4.2 %)	3 (4.2 %)	3 (4.2 %)	3 (4.2 %)	1	3 (3.9 %)	3 (4.4 %)	0.86

ICGR₁₅ indocyanine green retention rate at 15 min

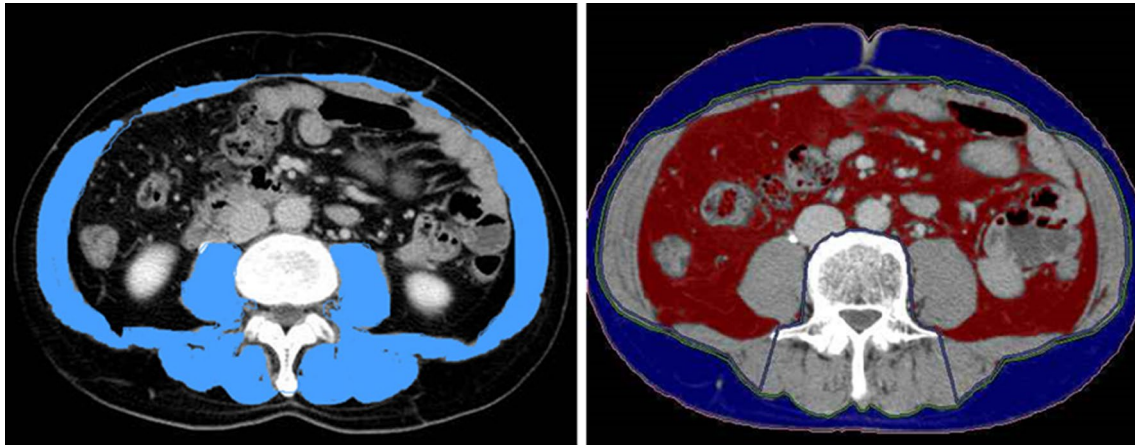


Fig. 1 Computed tomogram shows area of skeletal muscle mass (highlighted *blue*) and visceral fat amount (highlighted *red*) in L3 region. Areas of skeletal muscle mass and visceral fat amount were measured using the Synapse Vincent system. Skeletal muscle was

identified and quantified by Hounsfield unit (HU) thresholds of -29 to $+150$. Areas of visceral fat were calculated by measuring pixels with densities in the range of -190 to -30 HU

Results

Perioperative and postoperative outcomes

Of the 144 patients, 108 (75 %) were male and 36 (25 %) were female. The details of peri- and postoperative outcomes are described in Table 1. Serious postoperative complications, defined as grade III or greater (IV and V), occurred in 43 of the 144 patients (30 %). Liver-related morbidity occurred in 11 patients (7.6 %) and perioperative death in 8 (5.6 %), all of whom died of liver failure. Operative methods and diagnosis are shown in Table S1 (supporting information).

Sarcopenia and visceral fat amounts

The median amounts of skeletal muscle tissue were $43.2 \text{ cm}^2/\text{m}^2$ in men and $35.3 \text{ cm}^2/\text{m}^2$ in women. Using cutoff values of 103 cm^2 for men and 69 cm^2 for women, 69 patients (47.9 %) had high amounts of visceral fat. Comparative analysis showed that patients with sarcopenia and a low amount of visceral fat amount had a significantly lower body mass index (BMI) (Table 1). There were correlations among total skeletal muscle, BMI, and visceral fat amount (Fig. 2). Other factors such as age, sex, hepatitis, preoperative therapy, tumor size, number of tumors, tumor markers, and diagnosis were not related to the presence of sarcopenia or the amount of visceral fat. Additional analysis of the clinical significance of sarcopenia and visceral fat amount was performed in elderly patients aged more than 70 years. In this group, patients with sarcopenia and low visceral fat amount were significantly older and had significantly lower BMI (Table 2).

Impact of sarcopenia and visceral fat amount on surgical outcomes after major hepatectomy

The impact of sarcopenia or visceral fat amount on surgical outcomes after major hepatectomy was evaluated using the Pearson's chi-squared test (χ^2) (Table 1). The mortality rate was significantly higher in patients with sarcopenia than without sarcopenia ($P = 0.021$), whereas morbidity and liver-related morbidity rates did not differ significantly ($P = 0.58$, $P = 0.11$ respectively) (Table 1; Fig. S1A). In patients aged more than 70 years, the morbidity ($P = 0.046$), liver-related morbidity ($P = 0.025$), and mortality ($P = 0.0018$) rates were significantly higher in patients with than without sarcopenia. (Table 2, Figure S1B). In contrast, morbidity ($P = 0.5$), liver-related morbidity ($P = 0.9$), and mortality ($P = 0.37$) were similar in patients with high and low amounts of visceral fat (Table 1), even in the subgroup of patients aged more than 70 years (Table 2). Operation time, however, was significantly shorter in patients with low than high visceral fat amounts.

In univariable analysis, significant risk factors for mortality in all patients were low skeletal muscle mass, presence of HCV infections, long operative time, and high blood loss. In multivariable analysis, low skeletal muscle mass was identified as the risk factor in mortality (HR 4.3, $P = 0.038$) (Table 3).

In patients aged more than 70 years, the low skeletal muscle mass was a significant risk factor for morbidity and liver-related morbidity and mortality in univariable analysis. In multivariable analysis, low skeletal muscle mass was identified as the risk factor in all complications (morbidity:

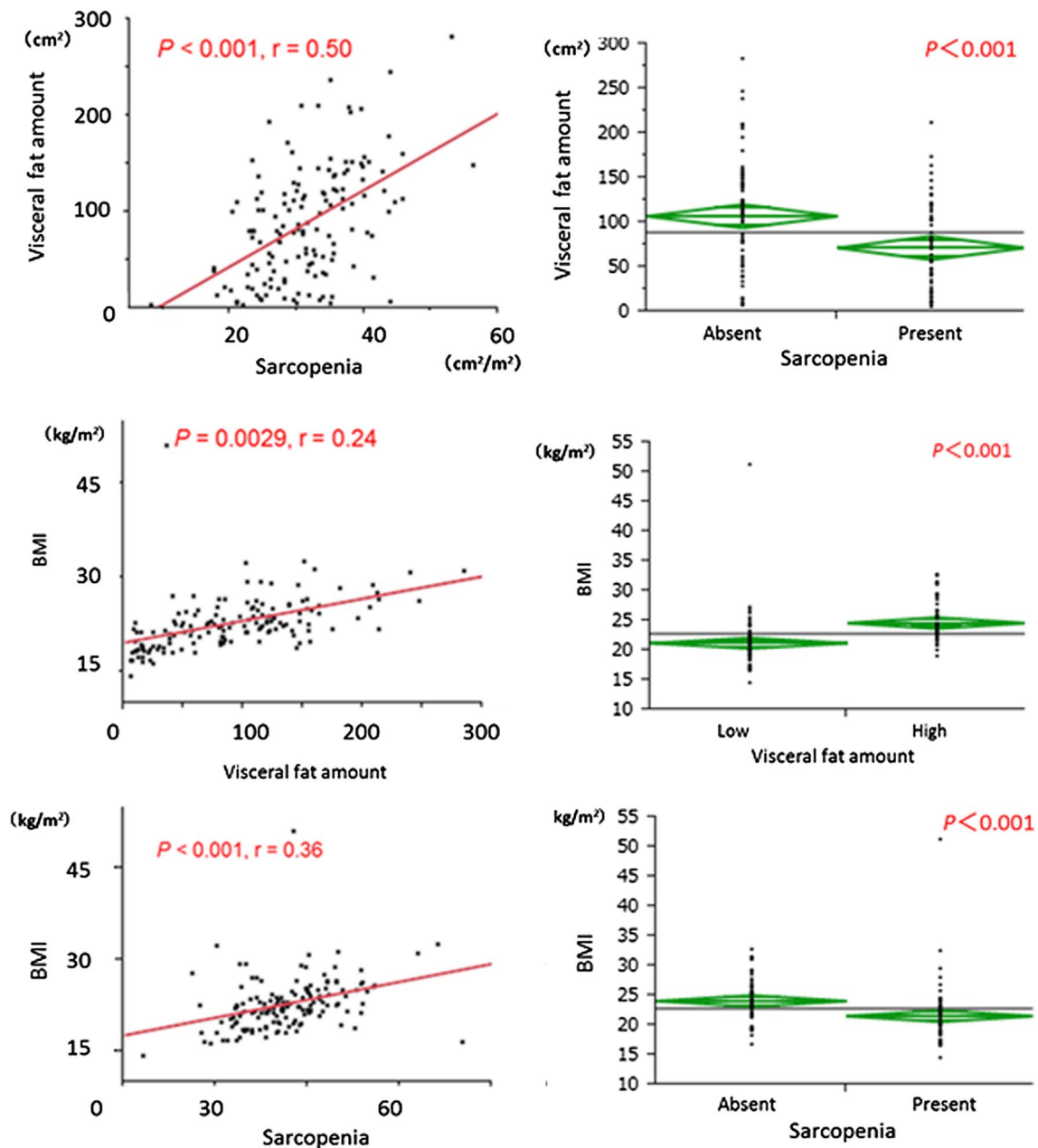


Fig. 2 Correlation analysis among sarcopenia, body mass index (BMI), and visceral fat amount. Positive correlations were determined among these three factors

HR 4.6, $P = 0.032$; liver-related morbidity: HR 6.54, $P = 0.011$; mortality: HR 6.54, $P = 0.011$) (Table 4).

Impact of sarcopenia and visceral fat amount on surgical outcomes after major hepatectomy in HCC patients

We also analyzed the impact of these factors in HCC patients only. The liver-related morbidity and mortality rates was significantly higher in patients with sarcopenia

than without sarcopenia ($P = 0.024$, $P = 0.01$ respectively), whereas the morbidity rate did not differ significantly ($P = 0.46$). In patients aged above 70 years, all rates were also significantly higher in patients with than without sarcopenia ($P = 0.035$, $P = 0.027$, $P = 0.0051$, respectively) (Table S2). The amount of visceral fat was not associated with morbidity, liver-related morbidity, and mortality rates in HCC patients (Table S2). We also examined univariable and multivariable analysis in all complications. In multivariable analysis, low skeletal muscle mass was

Table 2 Clinical and peri-operative factors relative to sarcopenia and visceral fat amount in patients aged more than 70 years

Clinical factors	Sarcopenia		<i>P</i>	Visceral fat amount		<i>P</i>
	Present (<i>n</i> = 24) (%)	Absent (<i>n</i> = 26) (%)		Low (<i>n</i> = 25) (%)	High (<i>n</i> = 25) (%)	
Age (years)	77.2 ± 3.1	74.3 ± 2.6	<0.001	76.7 ± 3.5	74.6 ± 2.5	0.017
Sex (male/female)	4/20	10/16	0.081	7/18	7/18	1
Skeletal muscle mass (cm ² /m ²)	34.2 ± 6.0	45.9 ± 10.1	<0.001	38.6 ± 9.1	42.0 ± 5.8	0.014
Body mass index (kg/m ²)	22.5 ± 7.4	24.6 ± 4.0	0.014	20.5 ± 3.3	23.7 ± 2.9	<0.001
Visceral fat amount (cm ²)	78.5 ± 58.5	110.5 ± 56.3	0.062	44.0 ± 27.3	143.6 ± 37.3	<0.001
Albumin (g/dl)	4.3 ± 0.3	4.1 ± 0.4	0.87	4.0 ± 0.4	4.0 ± 0.6	0.97
Total bilirubin (mg/dl)	0.9 ± 0.4	0.7 ± 0.2	0.73	0.8 ± 0.2	0.9 ± 0.4	0.39
Platelet count (× 10 ⁴ /μl)	18.2 ± 6.9	19.1 ± 6.7	0.28	16.4 ± 5.9	16.8 ± 6.0	0.45
ICGR ₁₅ (%)	10.9 ± 7.3	11.7 ± 9.1	0.84	13.8 ± 6.9	14.4 ± 10.2	0.9
Viral infection (HBV/HCV/nonBnonC)	14/24/0	14/18/8	0.027	14/20/6	14/22/2	0.45
Preoperative therapy (present/absent)	10/14	7/19	0.27	10/15	7/18	0.3
Tumor size (cm)	6.6 ± 3.7	6.4 ± 4.2	0.24	5.3 ± 2.8	6.3 ± 3.6	0.29
Number of tumors	2.1 ± 2.2	3.7 ± 1.2	0.53	1.9 ± 1.3	1.9 ± 1.0	0.56
Transfusion	1 (4.2 %)	0	0.235	0	1 (4 %)	0.235
Operative time (min)	417 ± 101	444 ± 109	0.71	422 ± 77	436 ± 97	0.64
Blood loss (ml)	968 ± 2425	437 ± 333	0.048	501 ± 470	431 ± 328	0.47
Morbidity	12 (50 %)	6 (23 %)	0.046	11 (44 %)	7 (28 %)	0.31
Liver-related morbidity	6 (25 %)	1 (3.8 %)	0.025	4 (16 %)	3 (12 %)	0.64
Mortality	6 (25 %)	0	0.0018	3 (12 %)	3 (12 %)	1

ICGR₁₅ indocyanine green retention rate at 15 min

identified as the risk factor for liver-related morbidity (HR 14.9, *P* = 0.0001) and mortality (HR 9.45, *P* = 0.0021) in HCC patients (Table S3), and in HCC patients aged more than 70 years (morbidity: HR 5.2, *P* = 0.023; liver-related morbidity: HR 8.5, *P* = 0.0035; mortality: HR 6.73, *P* = 0.0095; Table S4).

Discussion

The rates of sarcopenia are increasing in elderly patients who undergo major surgery, including hepatectomy. This study showed that sarcopenia is a useful predictive factor of mortality in patients undergoing major hepatectomy. Sarcopenia was a powerful predictor of postoperative complications, including morbidity, liver-related morbidity, and mortality, following major hepatectomy, especially in patients aged 70 years and older.

Sarcopenia is associated with aging, inactivity, and with a series of chronic diseases. Depletion of muscle mass was found to be a risk factor for perioperative infection, and sarcopenia was associated with increased length of hospital stay and requirements for prolonged rehabilitation [32]. In addition, sarcopenia was strongly associated with an increased risk of major postoperative complications in

patients who underwent hepatectomy for colorectal liver metastases [21]. As such, sarcopenia may be an objective measurement of frailty that might help predict the risk of perioperative morbidity. This study also showed that sarcopenia was significantly associated with postoperative complications (liver-related morbidity and mortality) in HCC patients (Table S2). Harimoto et al. [20] described the significant relationship between sarcopenia and long-term outcome in HCC patients with hepatic resection. Skeletal muscle was recently identified as an endocrine organ [33]. The cytokines and other peptides that are produced, expressed, and released by muscle fibers might influence the short-term and long-term outcome of HCC patients.

Selecting appropriate candidates for liver resection is therefore crucial to maximize the benefits derived from surgery [34, 35]. Hepatectomy is considered a high-risk operation in elderly patients, for both postoperative morbidity and mortality, because these patients already have low physical activity as a result of other diseases, including cardiac, pulmonary, and renal dysfunction and metabolic diseases [36, 37]. Sarcopenia may therefore be useful for identifying patients with low physical activity who are unable to tolerate major hepatectomy.

Several recent studies have reported that high visceral fat amount is associated with postoperative complications

Table 3 Univariable and multivariable analysis of clinical factors and mortality in all patients

Clinical factors	Morbidity			Liver-related morbidity			Mortality		
	Univariable analysis		P	Univariable analysis		P	Univariable analysis		P
	Hazard ratio	P		Hazard ratio	P		Hazard ratio	P	
Age ≥ 65 years	1.56 (0.76, 3.26)	0.23	2.55 (0.7, 12)	0.16	1.77 (0.35, 2.83)	0.213			
Sex (male)	1.23 (0.56, 1.66)	0.46	1.33 (0.74, 2.67)	0.57	1.45 (0.41, 2.43)	0.368			
Sarcopenia	1.22 (0.60, 2.51)	0.58	2.88 (0.79, 13.6)	0.11	5.32 (0.13, 7.65)	0.021	4.3 (0.12, 8.2)	0.038	
Body mass index ≤ 22.5 kg/m ²	0.94 (0.46, 1.91)	0.86	0.82 (0.23, 2.85)	0.75	0.53 (0.58, 1.72)	0.46			
Low visceral fat amount	0.78 (0.37, 1.61)	0.5	0.93 (0.26, 3.23)	0.9	0.80 (0.52, 1.94)	0.37			
Albumin ≥ 4 g/dl	0.48 (0.21, 1.03)	0.06	0.566 (0.12, 2.14)	0.41	0.82 (0.16, 3.47)	0.78			
Total bilirubin ≥ 0.7 mg/dl	0.57 (0.25, 1.23)	0.15	0.65 (0.13, 2.45)	0.53	0.75 (0.5, 2.0)	0.39			
Platelet count $\geq 16.8 \times 10^4/\mu\text{l}$	1.02 (0.49, 2.15)	0.95	2.53 (0.67, 12.2)	0.17	2.29 (0.31, 3.25)	0.13			
ICGR ₁₅ ≥ 10.7 %	0.57 (0.27, 1.21)	0.144	0.66 (0.16, 2.41)	0.53	0.51 (0.59, 1.69)	0.477			
HCV infection	1.40 (0.64, 2.98)	0.39	4.72 (1.34, 18.9)	0.016	12.4 (0.051, 19.4)	0.0004	11.0 (0.04, 22.3)	0.0009	
Preoperative therapy	1.33 (0.61, 2.83)	0.46	3 (0.855, 10.9)	0.085	3.69 (0.24, 4.15)	0.055			
Tumor size ≥ 5 cm	1.49 (0.71, 3.17)	0.29	1.43 (0.39, 5.82)	0.59	1.08 (0.25, 4.77)	0.91			
Multiple tumors	0.99 (0.47, 2.1)	0.98	0.57 (0.14, 2.11)	0.4	0.79 (0.52, 1.93)	0.374			
Transfusion	1.56 (0.2, 3.14)	0.48	1.98 (0.5, 7.1)	0.41	1.43 (0.11, 6.57)	0.41			
Operative time ≥ 418 min	2.26 (1.06, 4.96)	0.035	9.76 (1.76, 182)	0.0062	29.2 (2.55, 985)	0.019	5.72 (0.09, 10)	0.017	
Blood loss ≥ 400 ml	1.82 (0.86, 3.98)	0.12	9.78 (1.76, 183)	0.0062	5.07 (0.14, 7.35)	0.024			

Values in parentheses are 95 per cent confidence intervals
ICGR₁₅ indocyanine green dye retention test at 15 min

Table 4 Univariable and multivariable analysis of clinical factors and morbidity, liver-related morbidity and mortality in patients aged >70 years

Clinical factors	Morbidity		Liver-related morbidity		Mortality	
	Univariable analysis		Univariable analysis		Univariable analysis	
	Hazard ratio	P	Hazard ratio	P	Hazard ratio	P
Sex (male)	1.89 (0.38, 2.62)	0.17	1.23 (0.38, 2.6)	0.36	1.62 (0.48, 2.1)	0.49
Sarcopenia	3.3 (1.02, 11.9)	0.046	5.0 (1.21, 19.4)	0.032	9.7 (0.28, 3.55)	0.0018
Body mass index ≤ 22.4 kg/m ²	0.88 (0.57, 1.76)	0.35	1.04 (0.19, 5.29)	0.96	0.69 (0.12, 4.11)	0.67
Low visceral fat amount	0.42 (0.05, 3.25)	0.31	0.61 (0.02, 8.21)	0.64	0.95 (0.17, 6.22)	0.96
Albumin ≥ 4 g/dl	1.03 (0.37, 3.99)	0.76	1.0 (0.11, 2.1)	1.0	1.0 (0.17, 5.95)	1.0
Total bilirubin ≥ 0.7 mg/dl	0.52 (0.04, 5.35)	0.51	0.35 (0.12, 2.13)	0.16	0.24 (0.01, 1.67)	0.16
Platelet count $\geq 17.1 \times 10^4/\mu\text{l}$	0.68 (0.22, 3.1)	0.38	0.31 (0.02, 2.54)	0.133	0.23 (0.06, 1.91)	0.13
ICGR ₁₅ ≥ 10.3 %	0.39 (0.03, 1.56)	0.13	0.36 (0.02, 1.54)	0.133	0.22 (0.011, 1.52)	0.13
HCV infection	2.11 (0.42, 2.39)	0.15	6.67 (0.089, 11.2)	0.0098	11.6 (6.6, 15.1)	0.0007
Preoperative therapy	1.91 (0.55, 6.71)	0.31	6.01 (0.12, 8.24)	0.0114	8.23 (3.81, 8.69)	0.0041
Tumor size ≥ 5 cm	4.15 (1.2, 16.1)	0.024	5.0 (1.21, 19.4)	0.025	4.6 (0.05, 20.4)	0.032
Multiple tumors	1.3 (0.39, 4.32)	0.68	1.05 (0.18, 6.26)	0.96	1.05 (0.18, 6.26)	0.96
Transfusion	1.12 (0.09, 11.4)	0.36	2.04 (0.23, 9.18)	0.63	1.98 (0.21, 4.88)	0.63
Operative time ≥ 421 min	1.98 (0.6, 6.8)	0.26	3.69 (0.15, 6.67)	0.055	3.69 (0.15, 6.67)	0.055
Blood loss (ml) ≥ 400 ml	1.69 (0.51, 5.74)	0.39	4.37 (0.13, 7.81)	0.037	4.37 (0.13, 7.81)	0.037
						8.23 (1.15, 8.69)
						4.6 (0.049, 20.4)
						6.54 (0.39, 7.13)
						0.011
						0.0041
						0.032
						0.0007
						0.96
						0.96
						0.63
						0.055
						0.037
						0.037

Values in parentheses are 95% confidence intervals
ICGR₁₅ indocyanine green dye retention test at 15 min

in patients with gastric and colon cancer [38, 39]. In contrast, BMI and visceral fat amount did not correlate with postoperative complications after pancreaticoduodenectomy for pancreatic adenocarcinoma [40]. Moreover, obesity was not a risk factor for postoperative complications or mortality in patients after hepatic resection [25, 41]. In the present study, however, there were significant correlations between total skeletal muscle and visceral fat amount; the presence of high visceral fat amount did not have an effect on surgical outcomes, except for operation time, after major hepatectomy. We think that this is because Japanese have less visceral fat than Western people.

The limitations of this study are that it is a retrospective study. A further prospective study is required to confirm our results.

In conclusion, sarcopenia was a risk factor for mortality after major hepatectomy. In elderly patients aged more than 70 years, sarcopenia was a powerful and useful indicator of postoperative complications, including morbidity, liver-related morbidity, and mortality, after major hepatectomy. In contrast, the amount of visceral fat did not affect any surgical outcomes except for operation time.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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