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# Impact of Sarcopenia as a Prognostic Factor on Reductive Hepatectomy for Advanced Hepatocellular Carcinoma

SATOSHI OMIYA[1], SHOHEI KOMATSU[1], MASAHIRO KIDO[1], KAORI KURAMITSU[1], HIDETOSHI GON[1], KENJI FUKUSHIMA[1], TAKESHI URADE[1], SHINICHI SO[1], KEITARO SOFUE[2], YOSHIHIKO YANO[3], YOSHITADA SAKAI[4], HIROAKI YANAGIMOTO[1], HIROCHIKA TOYAMA[1], TETSUO AJIKI[1] and TAKUMI FUKUMOTO[1]

[1]*Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan;*
[2]*Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Japan;*
[3]*Department of Internal Medicine, Division of Gastroenterology, Kobe University Graduate School of Medicine, Kobe, Japan;*
[4]*Division of Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Japan*

**Abstract.** *Background/Aim: Sarcopenia has been reported to be a significant prognostic factor in patients with hepatocellular carcinoma in recent years. This study aimed to clarify the prognostic significance of sarcopenia in advanced hepatocellular carcinoma treated with reductive hepatectomy. Patients and Methods: We retrospectively analyzed 93 patients who underwent reductive hepatectomy for advanced hepatocellular carcinoma. Results: Median survival time of the sarcopenia group (16.4 months) was significantly shorter than that of the non-sarcopenia group (20.4 months). The overall survival rates at 1, 3, and 5 years of the sarcopenia group were significantly lower than those of the non-sarcopenia group (57.9%, 8.6%, and 2.9% vs. 67.3%, 29.2%, and 15.7%, respectively; p=0.035). On multivariate analysis, sarcopenia was a significant risk factor of overall survival (hazard ratio=1.60, 95% confidence interval=1.00-2.56, p=0.049). Conclusion: Sarcopenia was a significant prognostic factor of survival after reductive hepatectomy in advanced hepatocellular carcinoma.*

Hepatocellular carcinoma (HCC) is the sixth most common malignancy and the fourth most common cause of cancer-related deaths worldwide and often develops in patients with chronic liver disease (1). Curative treatment options for HCC are limited to radiofrequency ablation (RFA), hepatectomy, or liver transplantation (2, 3). Of these, hepatectomy is the best curative and effective treatment in patients with potentially resectable HCC (4). Although hepatectomy in resectable HCC is the gold standard of treatment, the effectiveness of reductive hepatectomy with residual tumors in the remnant liver of advanced HCC remains controversial, and the therapeutic strategy has not been established (5-7).

The rationale of our study was that the expeditious local control of intrahepatic liver tumors may prolong survival; therefore, the existence of intrahepatic metastases is not a contraindication for hepatectomy. We have aggressively performed reductive hepatectomy in advanced HCC and reported supportive results (8-11). Based on accumulated experience, patient selection is an important issue regarding survival especially in this type of aggressive treatment.

The concept of sarcopenia, which was originally reported by Rosenberg in 1989 as an age-related decline in muscle mass (12), and later was defined by Cruz-Jentoft as a syndrome associated with an increased risk of adverse events, characterized by progressive and systemic loss of skeletal muscle mass and strength (13). Recently, has been drawing attention in several cancer treatments (14-17). Sarcopenia has been identified as an effective prognostic factor in hepatectomy for resectable HCC (18-20). However, no study has demonstrated the relationship between sarcopenia and reductive hepatectomy. This study aimed to evaluate the impact of sarcopenia on outcomes following reductive hepatectomy.

*Correspondence to:* Shohei Komatsu, MD, Ph.D., Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan. Tel: +81 783826302, Fax: +81 783826307, e-mail: komasho8@med.kobe-u.ac.jp

*Key Words:* Sarcopenia, skeletal muscle index, reductive hepatectomy, advanced hepatocellular carcinoma.

## Patients and Methods

*Patient population*. Between June 2002 and December 2017, 685 consecutive patients with HCC underwent initial hepatectomy at Kobe University Hospital (Hyogo, Japan). Their clinical data were retrieved from our database, and tumors were staged using the Barcelona Clinic Liver Cancer (BCLC) staging system (2). HCC was detected using dynamic contrast-enhanced computed tomography (CT), angio-CT, or magnetic resonance imaging (MRI). Preoperative evaluation, blood biochemical tests, viral serological tests, coagulation tests, serum alpha-fetoprotein (AFP) levels, and serum protein induced by vitamin K absence or antagonist II (PIVKA-II) levels were measured. Preoperative liver function was evaluated using the Child-Pugh class, indocyanine green retention rate at 15 minutes (ICG-R15), and 99mTc-galactosyl human serum albumin scintigraphy. Tumor invasion into the portal and hepatic veins was diagnosed based on imaging and surgical findings and classified into five types (Vp0-Vp4) and four types (Vv0-Vv3), respectively, according to the Japanese staging system (21). Major hepatectomy was defined as resection of two or more segments. Postoperative complications were graded based on the Clavien–Dindo classification, and grades ≥IIIa complications were considered as severe. Initial hepatectomy was indicated in patients who fulfilled the following criteria: 1) no prohibitive comorbidities, 2) Eastern Cooperative Oncology Group performance status (ECOG-PS) of 0-2; 3) Child–Pugh class A or B liver function; and 4) macroscopic resection of the targeted tumor could be proposed with an adequate future liver remnant volume as calculated by preoperative CT volumetry. This study was approved by the Ethics Committee of Kobe University Hospital (approval number: 200345), and all procedures were conducted in accordance with the ethical guidelines of the 1975 Helsinki Declaration. All patients provided written informed consent prior to the treatment.

*Treatment strategy*. The types of resections were divided into complete or reductive hepatectomies. The definitions of complete or reductive hepatectomies have been detailed previously (10). Reductive hepatectomy was proposed only if the vital poor prognostic factors could be eliminated by excision of the main tumor, and subsequent treatment of the residual tumors after hepatectomy was being considered.

Subsequent local treatments included our original percutaneous isolated hepatic perfusion (PIHP), transcatheter arterial chemoembolization (TACE), transhepatic arterial infusion (TAI), resection, RFA, and radiotherapy (conventional photon and particle therapy). Details of subsequent local treatment strategies have been previously reported (9, 11).

*Definition of sarcopenia and study design*. CT is the gold standard for measuring skeletal muscle mass, and the single-slice CT cross-sectional area at the third lumbar vertebra (L3) has been applied in many studies as a dependable method to estimate body composition (22). We evaluated the skeletal muscle based on the latest preoperative unenhanced CT images. Cross-sectional areas ($cm^2$) of skeletal muscles in the L3 region were analyzed using a commercially available workstation (Ziostation 2 type1000; Ziosoft, Tokyo, Japan). The skeletal muscles were measured using a software with Hounsfield unit (HU) thresholds of -29 to 150 (water is defined as 0 HU and air as 1,000 HU). The tissue boundaries were manually modified, if necessary. The cross-sectional areas ($cm^2$) of the skeletal muscles were automatically calculated (Figure 1). Muscle areas were standardized for height ($m^2$) to get the L3 skeletal muscle index (SMI; $cm^2/m^2$). In the present study, sarcopenia was defined as a low skeletal muscle mass, signified by a low preoperative SMI. The assessment criteria for low SMI were categorized according to the working group for the development of sarcopenia assessment criteria of the Japan Society of Hepatology. The cut-off values for low SMI in men and women were <42 $cm^2/m^2$ and <38 $cm^2/m^2$, respectively (23).

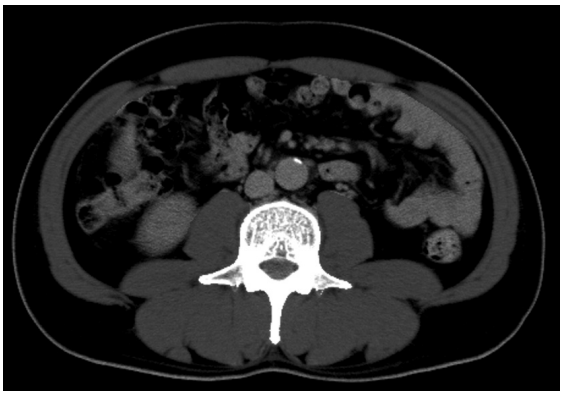

Figure 1.*Cross-sectional computed tomography showing the third lumbar vertebra. The red area shows the skeletal muscle area.*

Patients were divided into two groups due to the presence or absence of sarcopenia: the sarcopenia and the non-sarcopenia groups. The clinical background and rates of overall survival (OS) were compared between the two groups.

*Statistical analysis*. OS was defined as the interval between the date of first operation and the date of death or the last follow-up. Data are presented as mean±standard deviation (SD) for continuous variables. Continuous variables were analyzed using Mann-Whitney *U*-test, whereas categorical variables were analyzed using chi-squared or Fisher's exact test. OS rates were estimated using Kaplan–Meier analysis, and differences between curves were assessed using log-rank test. Cox proportional hazards model was employed for univariate and multivariate analyses. We considered any variable with $p<0.10$ in the univariate analysis to be a candidate for multivariate analysis using the Cox proportional hazards model. $p<0.05$ was considered statistically significant. All statistical data were generated using the JMP version 15 software (SAS Institute, Cary, NC, USA).

## Results

*Patient characteristics*. A total of 592 patients underwent complete hepatectomy, and 93 patients underwent reductive hepatectomy. The baseline characteristics of the 93 patients included in this study are outlined in Table I. Thirty-eight patients (41%) were classified into the sarcopenia group and 55 (59%) into the non-sarcopenia group. The sarcopenia group had a lower body mass index (BMI) ($p<0.0001$) than those in the non-sarcopenia group. Sex, patient age, etiology

Table I. *Baseline characteristics of 93 patients with advanced hepatocellular carcinoma who underwent reductive hepatectomy.*

| Variables | Total (n=93) | Sarcopenia (n=38) | Non-sarcopenia (n=55) | *p*-Value |
|---|---|---|---|---|
| Gender, male/female | 81/12 | 30/8 | 51/4 | 0.064 |
| Age, mean (SD), yr | 61.0 (13.5) | 61.1 (13.7) | 61.0 (13.3) | 0.983 |
| Etiology of liver disease | | | | 0.256 |
| HBV and / or HCV | 64 | 29 | 35 | |
| Others | 29 | 9 | 20 | |
| BMI, mean (SD), kg/m2 | 21.9 (3.0) | 20.0 (0.5) | 23.2 (0.4) | <0.0001 |
| ECOG-PS, 0/1 | 91/2 | 36/2 | 55/0 | 0.164 |
| Child-Pugh class, A/B | 82/11 | 34/4 | 48/7 | 0.747 |
| ALBI score, median (SD) | –2.39 (0.47) | –2.39 (0.46) | –2.38 (0.48) | 0.914 |
| ICG-R15, mean (SD), % | 13.8 (7.7) | 13.2 (8.2) | 14.2 (7.4) | 0.515 |
| PLT, mean (SD), $\times 10^4/mm^3$ | 18.4 (9.6) | 20.1 (12.1) | 17.3 (7.5) | 0.210 |
| Serum AFP level, mean (SD), ng/dl | 106,414 (467,477) | 104,178 (306,916) | 108,005 (553,446) | 0.967 |
| Serum PIVKA-II level, mean (SD), mAU/ml | 18,868 (38,689) | 19,901 (37,033) | 18,134 (39,816) | 0.832 |
| Maximal tumor size, mean (SD), cm | 8.81 (4.60) | 9.06 (4.18) | 8.63 (4.87) | 0.664 |
| Number of tumors | | | | 0.850 |
| Within 3 | 18 | 7 | 11 | |
| More than 4 | 75 | 31 | 44 | |
| Distribution of tumors | | | | 0.151 |
| Unilobar | 15 | 9 | 6 | |
| Bilobar | 78 | 29 | 49 | |
| Macroscopic vascular invasion | | | | 0.856 |
| Vp0 and Vv0 | 43 | 18 | 25 | |
| Others | 50 | 20 | 30 | |
| BCLC stage, B/C | 37/56 | 14/24 | 23/32 | 0.671 |

BMI: Body mass index; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; ALBI score: albumin-bilirubin score; ICG-R15: indocyanine green retention test at 15 min; PLT: platelet count; AFP: α-fetoprotein; PIVKA-II: protein induced by vitamin K absence or antagonist II; BCLC: Barcelona Clinic Liver Cancer.

of liver disease, BMI, ECOG-PS, Child-Pugh class, albumin-bilirubin (ALBI) score, ICG-R15, platelet count, serum AFP level, serum PIVKA-II level, maximum tumor size, number of tumors, tumor distribution, macroscopic vascular invasion, and BCLC stage were not significantly different between the two groups.

The treatment data of the 93 patients are summarized in Table II. Subsequent local treatments for remnant liver tumors after reductive hepatectomy were undertaken in 78 patients: 59 patients (53%) with PIHP, 22 (24%) with TACE or TAI, 6 (6%) with radiotherapy, and 1 (1%) with resection. The remaining 15 patients [6 patients (16%) in the sarcopenia group and 9 patients (16%) in the non-sarcopenia group] did not receive subsequent local treatments. Surgical procedure and operative blood loss did not differ significantly between the two groups.

The representative case after reductive hepatectomy and subsequent local treatments are shown in Figure 2A-C. Preoperative CT showed a large tumor and multiple intrahepatic metastases (Figure 2A). Postoperative CT showed multiple residual tumors in the remnant liver after right lobe hepatectomy (Figure 2B). Post-PIHP CT showed a complete response after PIHP, without apparent signs of recurrence in the remnant liver (Figure 2C).

*Outcomes of sarcopenia and non-sarcopenia patients*. The median survival time (MST) of the entire cohort was 17.9 months, and the 1-, 3-, and 5-year OS rates were 63.4%, 20.7%, and 10.4%, respectively. The sarcopenia group showed a worse OS than the non-sarcopenia group, with MST of 16.4 months, and 1-, 3-, and 5-year OS rates of 57.9%, 8.6%, and 2.9% *vs*. MST of 20.4 months and 67.3%, 29.2%, and 15.7%, respectively (log-rank $p=0.035$) (Figure 3).

The postoperative morbidity rate in all cohorts was 49% (n=46). There were no significant differences in the morbidity rates between the two groups (50% *vs*. 49%, $p=0.931$). Severe postoperative complication rates were also not statistically significantly different between patients with and without sarcopenia (29% *vs*. 16%, $p=0.147$) (Table II).

*Prognostic analyses for overall survival*. Univariate analysis showed that the significant prognostic factors for OS were sarcopenia [hazard ratio (HR)=1.60, 95%CI=1.03-2.49, $p=0.037$], serum AFP level (HR=1.72,

Table II. *Perioperative outcomes of 93 patients with advanced hepatocellular carcinoma who underwent reductive hepatectomy.*

| Variables | Total (n=93) | Sarcopenia (n=38) | Non-sarcopenia (n=55) | *p*-Value |
|---|---|---|---|---|
| Surgical procedure | | | | 0.988 |
| Minor | 27 | 11 | 16 | |
| Major | 66 | 27 | 39 | |
| Operative blood loss, Mean (SD), ml | 1,484 (1,265) | 1,330 (1,170) | 1,587 (1,325) | 0.341 |
| Subsequent local treatments | | | | 0.765 |
| PIHP | 49 | 20 | 29 | |
| TACE/TAI | 22 | 8 | 14 | |
| RT | 6 | 3 | 3 | |
| Resection | 1 | 1 | 0 | |
| No treatment | 15 | 6 | 9 | |
| Clavien–Dindo classification | | | | 0.200 |
| None | 47 | 19 | 28 | |
| I or II | 26 | 8 | 18 | |
| More than III | 20 | 11 | 9 | |

PIHP: Percutaneous isolated hepatic perfusion; TACE: transcatheter arterial chemoembolization; TAI: transhepatic arterial infusion; RT: radiation therapy.

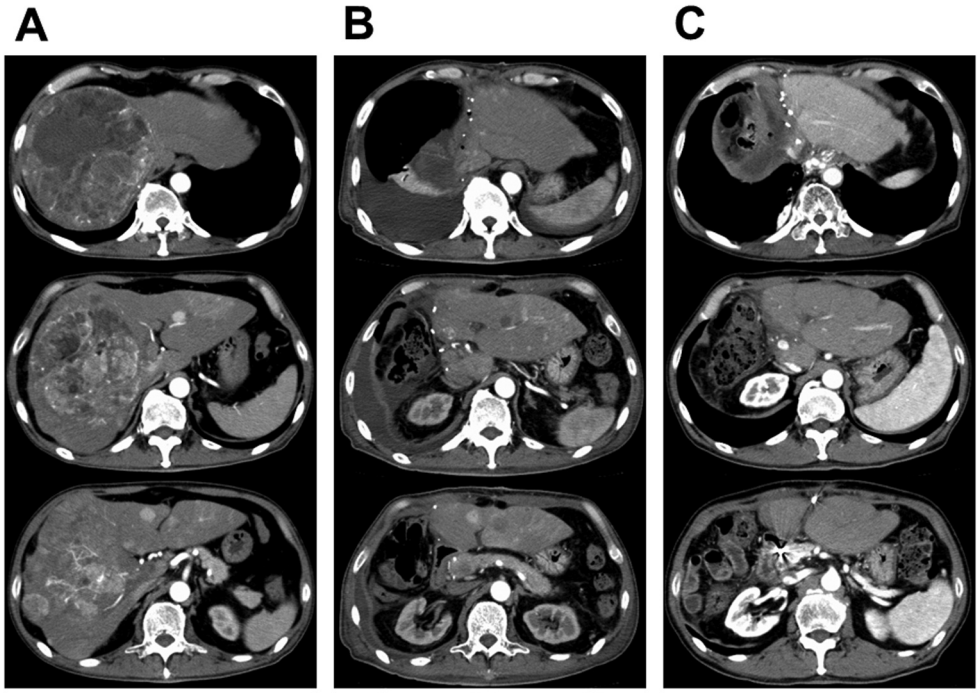


Figure 2. *The representative case after reductive hepatectomy and subsequent local treatments. (A) Preoperative contrast-enhanced computed tomography shows multiple tumors. (B) Postoperative contrast-enhanced computed tomography shows residual tumors after right lobe hepatectomy. (C) Post-percutaneous isolated hepatic perfusion (PIHP) contrast-enhanced computed tomography shows the complete response after PIHP.*

95%CI=1.10-2.70, $p$=0.018), BCLC stage (HR=1.58, 95%CI=1.00-2.48, $p$=0.049), and subsequent local treatments (HR=8.30, 95%CI=4.46-15.4, $p$<0.001) (Table III). sex, patient age, etiology of liver disease, BMI, ECOG-PS, Child-Pugh class, ALBI score, ICG-R15, platelet count, serum PIVKA-II level, maximal tumor size, number of tumors, distribution of tumors, macroscopic vascular invasion, surgical procedure, operative blood loss,

Table III. *Prognostic analyses for overall survival in entire cohort*.

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95%CI | *p*-Value | Hazard ratio | 95%CI | *p*-Value |
| Gender (female) | 0.80 | 0.39-1.67 | 0.556 | | | |
| Age (≥65 yr) | 0.87 | 0.57-1.34 | 0.540 | | | |
| Etiology of liver disease (HBV and/or HCV) | 1.25 | 0.78-2.02 | 0.352 | | | |
| BMI (≥25 kg/m$^2$) | 0.67 | 0.37-1.22 | 0.191 | | | |
| ECOG-PS (1) | 1.60 | 0.39-6.60 | 0.517 | | | |
| Child-Pugh class (B) | 1.12 | 0.59-2.13 | 0.719 | | | |
| ALBI score (≥–2.270) | 1.09 | 0.70-1.68 | 0.701 | | | |
| ICG-R15 (≥15 %) | 0.90 | 0.57-1.42 | 0.650 | | | |
| PLT (≤10×10$^4$/mm$^3$) | 0.74 | 0.40-1.35 | 0.321 | | | |
| Serum AFP level (>500 ng/dl) | 1.72 | 1.10-2.70 | 0.018 | 1.63 | 1.00-2.65 | 0.049 |
| Serum PIVKA-II level (≥40 mAU/ml) | 1.23 | 0.30-5.02 | 0.773 | | | |
| Maximal tumor size (≥8 cm) | 1.20 | 0.78-1.84 | 0.416 | | | |
| Number of tumors (≥4) | 1.36 | 0.78-2.35 | 0.276 | | | |
| Distribution of tumors (Bilobar) | 0.67 | 0.35-1.26 | 0.213 | | | |
| Macroscopic vascular invasion (others) | 1.47 | 0.94-2.28 | 0.089 | 1.05 | 0.36-3.04 | 0.931 |
| BCLC stage (C) | 1.58 | 1.00-2.48 | 0.049 | 1.11 | 0.38-3.29 | 0.849 |
| Surgical procedure (major) | 1.40 | 0.87-2.25 | 0.163 | | | |
| Operative blood loss (≥1,500 ml) | 1.03 | 0.66-1.61 | 0.909 | | | |
| Subsequent local treatments (no treatment) | 8.30 | 4.46-15.4 | <0.001 | | | |
| Clavien–Dindo classification (≥III) | 1.50 | 0.90-2.51 | 0.123 | | | |
| Sarcopenia (positive) | 1.60 | 1.03-2.49 | 0.037 | 1.60 | 1.00-2.56 | 0.049 |

BMI: Body mass index; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; ALBI score: albumin-bilirubin score; ICG-R15: indocyanine green retention test at 15 min; PLT: platelet count; AFP: α-fetoprotein; PIVKA-II: protein induced by vitamin K absence or antagonist II; BCLC: Barcelona Clinic Liver Cancer; PIHP: percutaneous isolated hepatic perfusion.

Table IV. *Prognostic analyses for overall survival in sarcopenia group*.

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Hazard ratio | 95%CI | *p*-Value | Hazard ratio | 95%CI | *p*-Value |
| Gender (female) | 0.67 | 0.28-1.63 | 0.376 | | | |
| Age (≥65 yr) | 0.78 | 0.40-1.50 | 0.452 | | | |
| Etiology of liver disease (HBV and/or HCV) | 0.84 | 0.39-1.80 | 0.651 | | | |
| BMI (≥25 kg/m$^2$) | 0.95 | 0.29-3.13 | 0.933 | | | |
| ECOG-PS (1) | 1.28 | 0.30-5.49 | 0.736 | | | |
| Child-Pugh class (B) | 4.46 | 1.45-13.7 | 0.009 | 3.53 | 1.09-11.4 | 0.035 |
| ALBI score (≥-2.270) | 1.24 | 0.62-2.48 | 0.552 | | | |
| ICG-R15 (≥15 %) | 1.53 | 0.71-3.31 | 0.282 | | | |
| PLT (≤10×10$^4$/mm$^3$) | 0.95 | 0.29-3.13 | 0.932 | | | |
| Serum AFP level (>500 ng/dl) | 1.81 | 0.91-3.60 | 0.093 | 1.56 | 0.76-3.22 | 0.228 |
| Maximal tumor size (≥8 cm) | 0.57 | 0.28-1.15 | 0.116 | | | |
| Number of tumors (≥4) | 0.78 | 0.34-1.81 | 0.566 | | | |
| Distribution of tumors (Bilobar) | 0.97 | 0.33-2.78 | 0.948 | | | |
| Macroscopic vascular invasion (others) | 1.00 | 0.51-1.97 | 1.000 | | | |
| BCLC stage (C) | 0.79 | 0.40-1.59 | 0.516 | | | |
| Surgical procedure (major) | 1.19 | 0.57-2.49 | 0.639 | | | |
| Operative blood loss (≥1,500 ml) | 0.69 | 0.33-1.45 | 0.331 | | | |
| Subsequent local treatments (no treatment) | 8.76 | 3.01-25.4 | <0.001 | | | |
| Clavien–Dindo classification (≥III) | 0.87 | 0.40-1.91 | 0.728 | | | |

BMI: Body mass index; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; ALBI score: albumin-bilirubin score; ICG-R15: indocyanine green retention test at 15 min; PLT: platelet count; AFP: α-fetoprotein; PIVKA-II: protein induced by vitamin K absence or antagonist II; BCLC: Barcelona Clinic Liver Cancer; PIHP: percutaneous isolated hepatic perfusion.

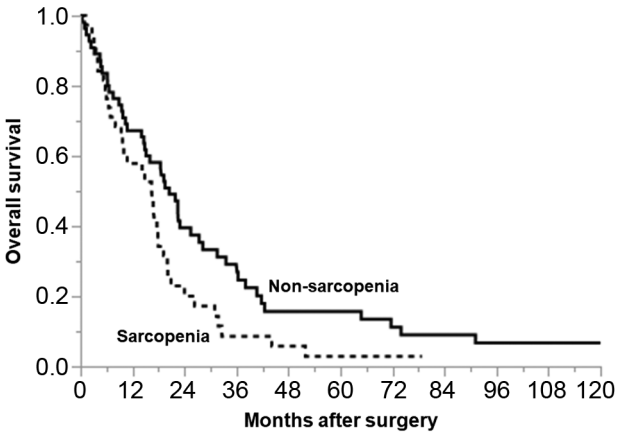


Figure 3. *Kaplan–Meier curve showing overall survival in sarcopenia and non-sarcopenia groups.*

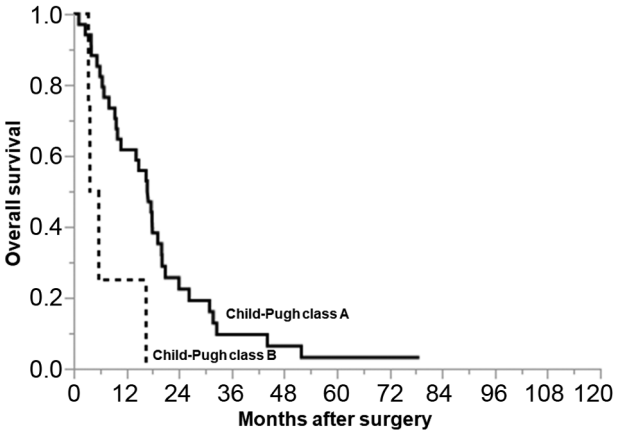


Figure 4. *Kaplan–Meier curve showing overall survival in sarcopenia group based on Child-Pugh class.*

and postoperative complications were not independent prognostic factors for OS.

Multivariate analysis showed that sarcopenia (HR=1.60, 95%CI=1.00-2.56, $p$=0.049) and serum AFP level (HR=1.63, 95%CI=1.00-2.65, $p$=0.049) were independent risk factors for OS (Table III).

*Prognostic analyses of sarcopenia group*. Further analyses focusing on the survival of the sarcopenia group are shown in Table IV. Univariate analysis showed that the significant prognostic factors for OS were Child-Pugh class B (HR=4.46, 95%CI=1.45-13.7, $p$=0.009) and subsequent local treatments (HR=8.76, 95%CI=3.01-25.4, $p$<0.001) (Table IV). Multivariate analysis showed that Child-Pugh class B (HR=3.53, 95%CI=1.09-11.4, $p$=0.035) was the only independent significant risk factor for OS (Table IV).

The patients in Child-Pugh class B group showed a worse OS than those in the Child-Pugh class A group, with an MST of 4.6 months, and 1-, 3-, and 5-year OS rates of 25.0%, 0%, and 0% *vs*. MST of 16.9 months and 61.8%, 9.6%, and 3.2%, respectively (log-rank $p$=0.004) (Figure 4).

## Discussion

The results of our retrospective study clearly indicated that sarcopenia was a significant prognostic factor for survival after reductive hepatectomy in advanced HCC. Furthermore, patients in the sarcopenia group with Child-Pugh class B disease were associated with a poor prognosis. To the best of our knowledge, this is the first report to demonstrate the relationship between sarcopenia and prognosis after reductive hepatectomy.

The mechanisms of the association between sarcopenia and the increased risk of mortality are poorly understood. Muscle mass declines owing to growth hormone secretion, and pulsatility decreases with age, especially above 50 years of age (24). Moreover, patients with liver cirrhosis have a high prevalence of sarcopenia (25). In recent years, chronic systemic inflammatory response has been clearly associated with subsequent poor outcomes, malnutrition and dysfunction in patients with cancer (26, 27). Sarcopenia is mentioned to be closely related in systemic inflammation (28). Skeletal muscle produces proteins with autocrine, paracrine, and endocrine effects including cytokines and other inflammatory markers, which cause systemic inflammatory effects (29). Based on these findings, various mechanisms explain the association between sarcopenia and poor prognosis after hepatectomy in HCC. The present study revealed that Child-Pugh class B could be a risk factor of survival in the sarcopenia group. It may be important to consider these factors if patients were classified in the sarcopenia group, and it may be required to reconsider the indications for aggressive strategy including reductive hepatectomy.

Palliative treatments such as TACE, TAI, and systemic chemotherapy are suitable for patients with BCLC stage B and C diseases and are considered as the best treatment options; however, the outcomes are not satisfactory (30, 31). In recent years, with the advent of new drugs such as lenvatinib (32) and atezolizumab with bevacizumab (33), we are entering a new era of multimodal chemotherapy. However, the patients in BCLC stages B and C are heterogeneous, and there always exists a population who can benefit from hepatectomy. The present study indicated that reductive hepatectomy in patients with sarcopenia requires careful attention, but it may be actively considered in patients without sarcopenia or some patients with sarcopenia.

Sarcopenia has been reported to be a significant prognostic factor not only in surgery, but also in other modalities (34-37). However, considering the invasive nature of surgical intervention, especially in advanced tumor status requiring reductive hepatectomy, a cautious approach is necessary for its indication. Preoperative evaluation of sarcopenia is an effective finding to clarify the indications for reductive hepatectomy. With the increase in the availability of various options in the multidisciplinary treatment of HCC in recent years, sarcopenia is expected to play an important role in selecting treatment options.

Our study has several limitations. The present study was retrospective and a strong selection bias in patient population might exist. Skeletal muscle strength was not investigated because of the retrospective nature of the study, and the relationship between this parameter and prognosis could not be analyzed. Further research is needed to address these limitations.

In conclusion, the present study demonstrated that sarcopenia is a significant and independent prognostic factor for advanced HCC after reductive hepatectomy. Preoperative evaluation of sarcopenia can be effective in risk assessment and clinical decision-making for patient selection.

## Conflicts of Interest

The Authors report no conflicts of interest in relation to this study.

## Authors' Contributions

Study design; Omiya S, Komatsu S. Data collection; Kido M, Kuramitsu K, Gon H, Fukushima K, Urade T, So S. Article preparation and review; Sofue K, Yano Y, Sakai Y, Yanagimoto H, Toyama H, Ajiki T. Supervision; Fukumoto T.

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