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Influencia de la fuerza de empuñadura en las complicaciones posoperatorias y la supervivencia en pacientes con cáncer de hígado primario

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ABSTRACT

Objectives: the impact of handgrip strength (HGS) on postoperative complications and long-term survival following hepatectomy in patients with primary liver cancer (PLC) remains unclear. This study aimed to evaluate the influence of HGS on postoperative complications and overall survival in patients with PLC.

Methods: in total, 298 patients with PLC who underwent liver resection were included in the prospective cohort study. Baseline, surgical, and histopathological factors were analyzed using univariate and multivariate analyses to identify risk factors for postoperative complications and mortality.

Results: the incidence of major postoperative complications was 40.3 % and 24.6 % in the low and high HGS groups, respectively. During the median follow-up period of 28.8 months, 57 patients (19.1 %) died. patients with low HGS demonstrated a significantly shorter median overall survival compared to those with high HGS ($p < 0.001$). Short-term analysis revealed that low HGS ($p = 0.022$) and intraoperative blood loss (≥ 200 ml) ($p < 0.001$) were independently associated with postoperative complications. Furthermore, low HGS was identified as an independent predictor of poor overall survival in long-term survival analysis (p = 0.005).

Conclusions: preoperative HGS emerged as an independent factor for postoperative complications and a prognostic indicator of poor long-term outcomes in patients with PLC.

Keywords: Hand grip strength. Primary liver cancer. Nutrition assessment. Postoperative complications. Overall survival. Hepatectomy.

RESUMEN

Objetivos: el impacto de la fuerza de empuñadura (HGS) en las complicaciones posoperatorias y la supervivencia a largo plazo tras la hepatectomía en pacientes con cáncer de hígado primario (PLC) sigue siendo incierto. Este estudio tuvo como objetivo evaluar la influencia de la HGS en las complicaciones posoperatorias y la supervivencia global en pacientes con PLC.

Métodos: un total de 298 pacientes con PLC que se sometieron a resección hepática fueron incluidos en el estudio de cohorte prospectivo. Los factores basales, quirúrgicos e histopatológicos fueron analizados mediante análisis univariados y multivariados para identificar los factores de riesgo de complicaciones posoperatorias y mortalidad.

Resultados: la incidencia de complicaciones posoperatorias mayores fue del 40,3 % y 24,6 % en los grupos de HGS baja y alta, respectivamente. Durante el período de seguimiento mediano de 28,8 meses, 57 pacientes (19,1 %) fallecieron. Los pacientes con HGS baja mostraron una mediana de supervivencia global significativamente más corta en comparación con aquellos con HGS alta (p < 0,001). El análisis a corto plazo reveló que la HGS baja (p = 0,022) y la pérdida de sangre intraoperatoria (≥ 200 ml) (p < 0,001) se asociaron de forma independiente con complicaciones posoperatorias. Además, en el análisis de supervivencia a largo plazo, se identificó la HGS baja como un predictor independiente de una mala supervivencia global (p = 0,005).

Conclusiones: la HGS preoperatoria surgió como un factor independiente para las complicaciones posoperatorias y un indicador pronóstico de malos resultados a largo plazo en pacientes con PLC.

Palabras clave: Fuerza de empuñadura. Cáncer de hígado primario. Evaluación nutricional. Complicaciones posoperatorias. Supervivencia global. Hepatectomía.

INTRODUCTION

Primary liver cancer (PLC) ranks sixth in terms of occurrence, while its mortality rate ranks fourth globally, making it one of the most dangerous malignancies. According to Globocan 2018, approximately half of new PLC cases and related death were recorded in China (1). Hepatectomy is the mainstay of treatment for PLC (2). While advancements in surgical techniques, rapid recovery applications, and perioperative management have led to a reduction in recurrence and mortality after liver resection, postoperative complications still occur in 15 %-50 % of cases (3). Although new therapeutic modalities have been introduced for PLC, the overall survival rates remain poor (4).

Handgrip Strength (HGS) offers an invaluable and non-invasive approach to evaluating muscle function (5), predicting nutritional level and overall health status (6,7), as supported by existing research. Additional applications of HGS include the ability to detect early signs of malnutrition through its sensitivity to protein inactivation (8). In cancer patients, the significance of HGS has become evident, as it has been identified as a risk factor for postoperative complications (9,10), longer hospital stays (11) and treatment toxicity (12). Furthermore, the correlation between reduced muscle strength (measured by HGS) and higher mortality rates emphasizes the importance of this metric

(13,14). Hence, the HGS is a vital tool for assessing nutritional levels and predicting health outcomes.

Sarcopenia, a loss of skeletal muscle mass, has been the focus of recent PLC research regarding its impact on liver resection prognosis (15-17). Individuals with sarcopenia who undergo hepatic resection experience higher rates of major complications (17) and lower overall and recurrence-free survival compared to those without sarcopenia (15). The European Working Group on Sarcopenia in Older People revised its 2018 guidelines, stating that probable sarcopenia is identified by low muscle strength, with diagnosis confirmed by low muscle quantity or quality (18). The HGS measurement is a simple and cost-effective method that has long been used to objectively quantify muscle strength.

However, the direct correlation between HGS and postoperative outcomes after liver resection remains largely unexplored. Existing research is limited by its focus on the short- or long-term implications of HGS in this specific context. To bridge this knowledge gap, further investigations are required to better understand the extent to which HGS influences the outcomes of liver resection. It remains uncertain whether HGS can serve as a prognostic indicator in these settings; however, it has the potential to be a valuable and straightforward test. This study aimed to evaluate the impact of HGS on short- and long-term outcomes following hepatectomy in patients with PLC. Our hypothesis suggests that low preoperative HGS could serve as a risk factor for poorer prognosis in the postoperative period. However, there is limited research examining this specific relationship in the context of liver resection.

MATERIALS AND METHODS

Study design

We retrospectively evaluated 298 patients with primary liver cancer who underwent hepatectomy at the Tianjin Medical University Cancer Hospital, Tianjin, China, from April 2018 to December 2023. During this time period, HGS was measured in all included populations before surgery. The study inclusion criteria were as follows: age 18-80 years, pathological diagnosis of PLC, well-compensated liver function, no contraindications for surgery, and no obvious hydrothorax or hydroperitoneum. The exclusion criteria were: complication with other malignant tumors and metastatic liver cancer. This study was approved by the Ethics Committee of Tianjin Medical University Cancer Hospital (No. Lx20190814). The current data are part of a registration trial (Clinical Registration No. NCT04218253).

A self-designed questionnaire was used to collect information. The data included baseline demographic data, histopathological variables, nutritional statistics, and surgical data. Based on them, all patients were staged according to tumor lymph nodes metastasis stage (TNM). This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all the participants prior to their inclusion in the study.

Measurement of handgrip strength

The HGS was measured using an electronic hand dynamometer (EH101; CAMRY, Guangdong, China). The dynamometer used in this study had a measurement range of 0 to 99.9 kg, with a precision of 0.1 kg. To enhance the grip, the handle of the dynamometer was customized to fit the size of each individual's palm. During the measurement process, the participants were instructed to maintain an upright stance with their feet shoulder-width apart, while keeping the dynamometer at a distance from their bodies. All patients were measured twice per hand for more than 3 s, and the highest result among the four measurements was used as the hand grip strength value.

To define low Handgrip Strength (HGS), specific thresholds were established based on age and gender. Based on the study by Mauricio SF et al. (19), for individuals aged ≥ 60 years, low HGS was indicated by grip strength ≤ 30 kg for men and ≤ 20 kg for women. For individuals below the age of 60, thresholds were set below 36.7 kg for men and below 20.8 kg for women.

Assessment of Patient-Generated Subjective Global Assessment (PG-SGA)

Nutritional status was evaluated using the PG-SGA, which is widely used in clinical nutrition assessment (20) and is detailed at PT-Global, consisting of two parts. The first part contains weight history, diet intake, symptoms and functions and needs to be completed by the participant. The second part includes diseases, age, metabolic stress and physical examination and is filled up by the investigator. The PG-SGA (Patient-Generated Subjective Global Assessment) score is divided into three levels: A (0-1) represents good nutrition, B (2-8) indicates suspicious or mild to moderate malnutrition and C (≥ 9) indicates severe malnutrition.

Assessment of Nutritional Risk Assessment 2002 (NRS-2002)

NRS-2002 (Nutritional Risk Screening 2002) consists of three parts: disease severity score, nutritional status score and age. Given that all the patients underwent liver resection, the disease severity score was 2, ranging from 2 to 6. Remarkably, patients with a minimum NRS-2002 score of 3 were classified as having nutritional risk (21).

Outcomes

To determine the impact of the surgery, postoperative complications were assessed using the Clavien-Dindo classification, a recognized system that categorizes complications based on their severity. In this study, grade 2 or higher complications were deemed major complications, indicating their potential to significantly affect patient outcomes (22). The length of hospital stay, another crucial aspect of postoperative recovery, was measured from the day of operation until discharge. Subsequent follow-up appointments were scheduled at intervals of either 3 or 6 months to monitor progress and detect any potential complications or relapses in a timely manner. The last follow-up date was December 25, 2023. Overall survival (OS) was calculated from the date of surgery to the date of death from any cause.

Statistical analysis

Statistical analysis of the data was performed using SPSS software (version 22). Continuous variables were tested using the Student's t-test or the non-parametric Mann-Whitney U test, and categorical variables were analyzed using Pearson χ^2 or Fisher's exact test. Correlations between variables were analyzed using Spearman's correlation test. Binomial univariate logistic regression analyses were used to identify factors associated with the occurrence of postoperative complications. Factors with a *p*-value of less than 0.1 were entered into a multiple logistic regression model to identify which factors were significantly correlated with postoperative complications. Cox proportional hazards regression analyses were performed to identify prognostic factors for OS. Multivariate analysis was performed for the factors with $p < 0.1$ in a univariate analysis. To assess survival, we employed the Kaplan-Meier method and compared survival curves using log-rank tests. Statistical significance was set at $p \leq 0.05$.

RESULTS

Characteristics of participants

In this study, 298 patients were recruited, with males comprising 81.2 % (242) of the sample. Moreover, the participants in this study had a mean age of 58.57 ± 9.44 years. Participants were categorized into groups based on HGS: the low HGS group consisted of 62 patients (20.8 %), whereas the high HGS group included 236 patients (81.2 %). Table I shows the basic population characteristics of the patients divided by HGS.

Comparing the two groups, the low HGS group exhibited significantly lower weight ($p < 0.001$), body mass index (BMI) ($p < 0.001$), albumin (ALB) ($p <$

0.001) levels, hemoglobin (HGB) levels ($p = 0.001$), postoperative 5-day (POD5) ALB levels ($p = 0.011$), POD5 HGB levels ($p = 0.001$), a higher PG-SGA score ($p < 0.001$) and NRS-2002 score ($p = 0.001$), and higher TNM stage ($p = 0.024$), and longer postoperative hospital stay ($p = 0.031$) (Table I) were observed in the study participants. These findings indicate a clear association between HGS and various clinical parameters.

Exploring the nexus between handgrip strength and indices exploring nutrition

Table II presents the relationship between the HGS and nutrition-related indices. HGS was positively correlated with BMI, ALB, prealbumin (PA), and HGB and negatively correlated with the PG-SGA and NRS-2002 scores. Notably, HGS strongly correlated with HGB levels ($r = 0.416$, $p < 0.001$). When analyzing the data by sex, HGS showed the highest correlation with BMI ($r = 0.344$, $p < 0.001$). However, among the female participants, no statistically significant correlation was observed between HGS and any of the evaluated indices.

Low handgrip strength group shows elevated incidence of major complications

According to the Clavien-Dindo Classification (Table III), of the 83 patients examined, approximately 27.8 % encountered major complications. Notably, a higher occurrence of major complications (grade ≥ ¡ 2) was observed in the low HGS group than in the high HGS group. Specifically, 40.3 % of the patients in the low HGS group experienced major complications, while the incidence was lower at 24.6 % in the high HGS group. This discrepancy was statistically significant ($p = 0.014$). The subsequent table provides a breakdown of the complications according to age and sex (Supplementary Tables I and II).

Factors associated with postoperative complications in liver resection surgery

The univariate analysis revealed that several factors were significantly associated with postoperative complications (Table IV). These factors included the extent of resection (≥ 3 segments) ($p = 0.004$), intraoperative blood loss ≥ 200 ml ($p < 0.001$), lower HGS ($p = 0.015$) and higher TNM stage ($p = 0.047$). Additionally, laparotomy showed a trend towards significance with p-value below 0.1. Multivariate analysis revealed that blood loss (≥ 200 ml) (odds ratio [OR] = 2.81, 95 % CI: 1.60-4.93, $p < 0.001$) and low HGS (OR = 2.08, 95 % CI: 1.11-3.89, $p = 0.022$) were independently associated with postoperative complications. When grouped by age (Supplementary Tables III and IV), low HGS (OR = 3.10, 95 % CI: 1.40-6.82, $p = 0.005$) and intraoperative blood loss (≥ 200 ml) (OR = 3.02, 95 % CI: 1.53-5.96, $p = 0.001$) were significant risk factors for postoperative complications in the young age group.

Factors associated with survival in patients undergoing surgery

The median follow-up period was 28.8 months. The low HGS group had 22 deaths (mortality rate 35.48 %), whereas the high HGS group had 35 deaths (mortality rate 14.83 %). OS was significantly worse in the low HGS group than in the high HGS group (hazard ratio (HR) = 2.51, 95 % CI: 1.22-5.16, $p = 0.013$) (Fig. 1A). The median OS of patients with low HGS was 54.4 months (high HGS group not reached, $p < 0.001$). The survival curves demonstrated that an NRS-2002 score of ≥ 3 ($p = 0.013$), PG-SGA classification ($p = 0.003$) and serum albumin levels ≤ 40 ($p = 0.005$) were also associated with worse overall survival (OS) (Figs. 1 B-D).

Table V presents the results of the analysis of the prognostic factors for OS. In univariate analysis, the following factors were found to be statistically significant: extensive operation (≥ 3 segments) ($p = 0.017$), low HGS ($p < 0.001$), NRS-2002 score of ≥ 3 ($p = 0.014$), and occurrence of major postoperative complications ($p = 0.008$). The pathological type (hepatocellular carcinoma) showed a p value ≤ 0.1. Multivariate analysis concluded that only low HGS (HR = 2.29, 95 % CI: 1.29-4.07, $p = 0.005$) was a significant independent risk factor.

DISCUSSION

This study aimed to examine the influence of pre-operative Handgrip Strength (HGS) in patients diagnosed with primary liver cancer (PLC) and its impact on postoperative complications and overall survival (OS). Additionally, this study explored the correlation between the HGS and other nutritional assessment tools. Notably, the results indicated that low HGS and substantial intraoperative blood loss increased the risk of postoperative complications in patients with PLC. Furthermore, this study revealed that low HGS was an independent predictor of poor OS in patients with PLC. This investigation is the first to analyze the association between HGS and short- or long-term outcomes following hepatic resection in patients with PLC.

The HGS is an indicator that captures holistic muscle strength and is correlated with physical functionality (6). While the association between preoperative HGS and prognosis has been investigated in various cancer types, such as gastric (23), pancreatic (24), and esophageal cancers (9), limited attention has been given to its impact on Primary Liver Cancer. According to Sato et al. (9), HGS has been identified as a predictive factor for postoperative complications, specifically postoperative pneumonia, in males aged ≥ 70 years. However, this study did not find any significant correlation between HGS and postoperative complications in patients aged ≤ 70 years. Another study in 2022 (4) found that HGS, compared to other nutritional assessment tools, was independently associated with complication-free survival and approached significance for overall survival in patients with multiple liver cancer treatments (25). Thus, HGS has become a popular indicator for clinical assessment.

Furthermore, HGS has been suggested as a marker of aging and shown to influence the outcomes of various diseases (14,26). In this study, other nutritional assessment methods, such as NRS-2002 and BMI, did not predict postoperative complications in the final multivariate analysis. Univariate Cox analysis indicated that factors such as the extent of resection, major postoperative complications, and NRS-2002 scores ≥ 3 were related to shorter OS. Nevertheless, NRS-2002 scores were not significant prognostic factors in multivariate regression analysis. These findings highlight the beneficial use of HGS in identifying physical conditions among patients with PLC. Possible reasons for the superior predictive power of HGS over nutritional assessment tools include the fact that malnutrition and low HGS do not appear simultaneously (27). The HGS reflects the physical condition and illness status more accurately, making it a robust predictor of prognosis. For another, the current nutritional evaluation instruments may not possess the required sensitivity to detect slight variations in liver cancer prior to surgical intervention, while HGS might detect these changes earlier. Additionally, in the present study, an enhanced recovery protocol after surgery was applied, which possibly improve the patients' postoperative condition and eliminate the consequences of malnutrition. However, muscle function responds to early nutritional deprivation and recovery (5).

Baseline analysis showed significant associations between reduced HGS and indicators such as decreased body weight, lowered BMI, diminished albumin levels, elevated NRS-2002 scores, and increased PG-SGA scores. Further analysis revealed a negative relationship between the HGS and nutritional status, particularly in males. However, this relationship was not observed in females, likely attributed to the relatively small number of women in the study. Most studies have reported that individuals exhibiting elevated HGS demonstrate a reduced likelihood of malnutrition and nutritional vulnerability (28). As the liver is responsible for nutrient metabolism, malnutrition is a significant risk factor for liver cancer. It is important to pay attention to the nutritional status of these patients, as malnutrition can worsen muscle loss and lead to inflammation, thereby affecting their clinical outcomes. Therefore, the nutritional status of patients with liver cancer and low HGS should be closely monitored.

Sarcopenia is defined by the new edition of the European Working Group on Sarcopenia in Older People as a decline in muscle strength and muscle mass (29). Many studies have focused on the association between sarcopenia and short- (15) and long-term prognosis after hepatectomy in patients with liver cancer. Harimoto et al. (15,16) reported that sarcopenia is a prognostic factor for overall and recurrence-free survival in patients following partial hepatectomy. A French study showed that the difference in postoperative mortality and morbidity rates between sarcopenic and nonsarcopenic groups was insignificant (30); however, complications were not analyzed as key outcome variables in this study. Findings from Europe and America reached slightly different conclusions. A study conducted by Valero et al. (31) reported that severe complications (Clavien grade ≥ 3) occurred only in patients with sarcopenia. The differences can be explained by variations in race, heterogeneous cohorts and assessment methods. In summary, sarcopenia predicts a poor outcome after hepatectomy. Unfortunately, several components of sarcopenia such as muscle quantity or gait speed were not included in our study. Despite the potential clinical value of HGS and sarcopenia assessment, the use of sarcopenia is limited factors such as financial limitations and logistical intricacies pose challenges in implementing these findings into routine clinical practice.

In this study, the incidence of grade 2 or higher complications was 27.85 %, which is similar to that reported in a previous study (29 %) (30). To our knowledge, surgical complications are poor prognostic factors after surgery for hepatocellular carcinoma (HCC) (15). Yang et al. (32) showed that short-term postoperative complications of HCC affect the overall postoperative and recurrence-free survival. Medical teams have strived to reduce the incidence of complications. In addition, surgical blood loss (≥ 200 ml) was identified as an independent risk factor for complications. Intraoperative bleeding has been used to predict treatment outcomes (33), mortality and recurrence (34,35). Nevertheless, postoperative complications and intraoperative blood loss remain important concerns for patients undergoing hepatic resection, even though they do not have a significant effect on survival in the final prognostic analysis.

Clinical practice guidelines recommend evaluating patients with liver disease to assess malnutrition and sarcopenia before surgery. Appropriate management of sarcopenia can improve protein status and clinical outcomes (36,37). Early detection and treatment of low HGS using various strategies can enhance the postoperative outcomes in frail patients. Physical exercise has anti-catabolic and anabolic effects on muscles, releasing muscle factors that can positively affect treatment and cachexia (38,39). Additionally, enhancing muscle state through nutritional interventions and regular physical activity has the potential to influence both surgical results (40) and long-term survival (41,42). Pre-rehabilitation studies using resistance training have been shown to reduce postoperative complications in different diseases; however, their effect on poor prognosis resulting from low grip strength has not been studied.

One advantage of this study was that HGS and nutrition were assessed by a trained dietitian, thereby avoiding differences between evaluators. In addition, various preoperative nutritional assessment tools were used to comprehensively assess patients' overall preoperative status. Nevertheless, this study has some limitations. Progression-free survival data were unavailable. In future experimental designs, missing data will be accounted for, and a larger sample size will be used to determine reliable cutoff values for different sex and age groups. The findings from this study are not applicable to patients with advanced liver cancer, as they included only patients who underwent feasible surgical resection. Large observational studies are required to further analyze the association between handgrip strength and far-reaching results. Future studies should also explore whether perioperative muscle strength training can prolong the prognosis.

CONCLUSIONS

Preoperative HGS has been found to have negative effects on the present and future after surgical removal of the liver in individuals diagnosed with PLC. As a straightforward, uncomplicated and cost-effective measure of nutritional profile, HGS should be routinely measured before surgery. The use of HGS as a preoperative indicator can be easily implemented by any healthcare professional following the prescribed procedures. Consequently, it is recommended that HGS measurement becomes a regular practice, as it can provide valuable insights into patients' nutritional status prior to surgery.

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Table I. Sample demographic and clinical characteristics according to handgrip strength

Variables	**High HGS** ***n*** **= 236**	**Low HGS** ***n*** **= 62**	***p*-value**
Age (years)[a]	58.18 ± 9.16	60.05 ± 10.38	0.165
SEX (male)	190	52	0.546
Weight (kg)	71.59 ± 12.52	63.65 ± 9.42	< 0.001
BMI (kg/m^2)	24.81 ± 3.42	22.86 ± 3.04	< 0.001
PG-SGA	3.41 ± 2.47	4.79 ± 2.85	< 0.001
NRS-2002	2.42 ± 0.81	2.84 ± 0.98	0.001
ALB (g/L)	42.29 ± 3.92	39.99 ± 4.36	< 0.001
PA (g/L)	0.19 ± 0.05	0.18 ± 0.06	0.199
HGB (g/L)	144.89 ± 16.38	136.94 ± 20.00	0.001
HGS (kg)	38.01 ± 8.79	27.69 ± 6.38	< 0.001
Comorbidity	89	30	0.127
Laparoscope (minimal invasive approach)	59	13	0.509
Intraoperative blood loss (mL) ≥ 200	70	16	0.551
Extent of resection (≥ 3 segments)	71	24	0.195
TNM stage			
I	185	40	0.024
II-IV	51	22	
Operation time (min)	154.51 ± 61.29	151.39 ± 81.30	0.758
Histopathological type			
HCC	198	50	0.209
ICC	33	8	
cHCC-CC	5	4	
POD5 ALB (g/L)	34.91 ± 4.22	33.33 ± 4.56	0.011
POD5 PALB (g/L)	0.11 ± 0.04	0.10 ± 0.04	0.092
POD5 HGB (g/L)	124.15 ± 18.96	114.56 ± 21.36	0.001
Postoperative	8.68 ± 5.60	10.55 ± 7.48	0.031

hospital stay (day)			

BMI: body mass index; PG-SGA: Patient-Generated Subjective Global Assessment; NRS-2002: Nutritional Risk Screening 2002; ALB: albumin; PA: prealbumin; HGB: hemoglobin; HGS: handgrip strength; TNM: tumor lymph nodes metastasis stage; HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; cHCC-CC: combined hepatocellular carcinoma and cholangiocarcinoma; POD: postoperative day. [a]Means ± standard deviation or *n*. A bold *p*-value indicates statistical significance ($p < 0.05$). Fisher's exact test, Chi-squared test, Student's t-test or Mann-Whitney U test.

Table II. Correlation between handgrip strength and nutritional assessment methods

	All (*n* = 298)		**Male (*n* = 242)**		**Female (*n* = 56)**	
	r	***p*-value**	***r***	***p*-value**	***r***	***p*-value**
PG-SGA	-0.141	0.015	-0.170	0.008	-0.260	0.053
NRS-2002	-0.126	0.029	-0.177	0.006	-0.190	0.160
BMI	0.26	< 0.001	0.344	< 0.001	0.061	0.653
ALB	0.212	< 0.001	0.238	< 0.001	0.143	0.292
PA	0.226	< 0.001	0.176	0.007	0.168	0.216
HGB	0.416	< 0.001	0.226	< 0.001	0.059	0.664

BMI: body mass index; PG-SGA: Patient-Generated Subjective Global Assessment; NRS-2002: Nutritional Risk Screening 2002; ALB: albumin; PA: prealbumin; HGB: hemoglobin.

Table III. Postoperative complications (Clavien-Dindo classification)

Grade	**Total (*n*)**	**High HGS (*n* = 236)**	**Low HGS (*n* = 62)**	***p*-value**
Grade 0	100	77(32.6)	23(37.1)	0.004
Grade 1	115	101(42.8)	14(22.6)	
Grade 2	57	42(17.8)	15(24.2)	
Grade 3	20	14(5.9)	6(9.7)	
Grade 4	6	2(0.8)	4(6.5)	
≥ Grade 2	83	58(24.6)	25(40.3)	0.014

HGS: handgrip strength. The values given are number (%).

Table IV. Logistic regression of risk factors for major complications

variables	Univariate		Multivariate	
	OR (95 % CI)	*p*-value	OR (95 % CI)	*p*-value
Sex (male/female)	1.07(0.56,2.06)	0.843		
Age (≥ 65)	1.03(0.59,1.80)	0.926		
Laparotomy (yes)	1.82(0.95,3.48)	0.070	1.52(0.76,3.01)	0.235
Extent of operation Complex (≥ 3 segments)	2.18(1.29,3.69)	0.004	1.54(0.87,2.74)	0.141
Intraoperative blood loss (≥ 200 ml)	2.94(1.72,5.03)	<0.001	2.81(1.60,4.93)	<0.001
HGS (LOW)	2.07(1.15,3.73)	0.015	2.08(1.11,3.89)	0.022
Obesity (BMI ≥ 24)	0.79(0.48,1.32)	0.366		
NRS-2002 ≥ 3	1.43(0.86,2.37)	0.172		
Comorbidity (yes)	1.06(0.63,1.78)	0.821		
TNM stage (II-IV)	1.77(1.01,3.11)	0.047	1.38(0.75,2.56)	0.298
Pathological type (HCC)	0.63(0.33,1.20)	0.161		

HGS: handgrip strength; NRS-2002: Nutritional Risk Screening 2002; TNM: tumor lymph nodes metastasis stage; HCC: hepatocellular carcinoma.

Table V. Univariate and multivariate analysis concern overall survival

Variables	**Univariate**		**Multivariate**	
	HR (95 % CI)	***p*-value**	**HR (95 % CI)**	***p*-value**
Sex (1 = female)	1.30 (0.64, 2.66)	0.470		
Age (≥ 65)	1.08 (0.62, 1.88)	0.790		
Laparotomy (yes)	1.47 (0.74, 2.91)	0.270		
Extent of resection (≥ 3 segments)	1.90 (1.12, 3.22)	0.017	1.54 (0.86, 2.76)	0.144

Intraoperative blood loss (≥ 200 ml)	1.03 (0.58, 1.82)	0.920		
HGS (low)	2.73 (1.60, 4.67)	< 0.001	2.29 (1.29, 4.07)	0.005
Obesity (BMI ≥ 24)	0.74 (0.44, 1.24)	0.250		
NRS-2002 ≥ 3	1.95 (1.14, 3.33)	0.014	1.44 (0.82, 2.54)	0.251
CD ≥ 2	2.06 (1.21, 3.51)	0.008	1.44 (0.80, 2.59)	0.224
Comorbidity (yes)	1.08 (0.64, 1.82)	0.785		
TNM stage (II-IV)	1.06 (0.58, 1.95)	0.843		
Pathological type (HCC)	0.58 (0.31, 1.09)	0.089	0.74 (0.38, 1.43)	0.358

HGS: handgrip strength; NRS-2002: Nutritional Risk Screening 2002; CD: Clavien-Dindo classification; TNM: tumor lymph nodes metastasis stage; HCC: hepatocellular carcinoma.

Supplementary Table I. Postoperative complications by gender (Clavien-Dindo classification)

Grade	**Total**	**Male (*n* = 242)**	**Female (*n* = 56)**	***p*-value**
Grade 0	100	73	27	
Grade 1	115	101	14	
Grade 2	57	43	14	-
Grade 3	20	19	1	
Grade 4	6	6	0	
≥ Grade 2	83	68	15	0.843

Supplementary Table II. Postoperative complications by age (Clavien-Dindo

classification)				
Grade	Total	< 65 (*n* = 213)	≥ 65 (*n* = 85)	*p*-value
Grade 0	100	76	24	
Grade 1	115	78	37	
Grade 2	57	39	18	-
Grade 3	20	14	6	
Grade 4	6	6	0	
≥ Grade 2	83	59	24	0.926

Supplementary Table III. Logistic regression of risk factors for major complications in young group (age < 65) (*n* = 213)

Variables	**Univariate**		**Multivariate**	
	OR (95 % CI)	***p*-value**	**OR (95 % CI)**	***p*-value**
Sex (male/female)	1.04 (0.47, 2.31)	0.920		
Laparotomy (yes)	1.42 (0.69, 2.94)	0.344		
Extent of resection (≥ 3 segments)	2.18 (1.17, 4.06)	0.014	1.52 (0.76, 3.05)	0.238
Intraoperative blood loss (≥ 200 ml)	3.29 (1.74, 6.20)	< 0.001	3.02 (1.53, 5.96)	*0.001*
HGS (LOW)	3.38 (1.63, 6.98)	0.001	3.10 (1.40, 6.82)	*0.005*
Obesity (BMI ≥ 24)	0.66 (0.36, 1.21)	0.183		
NRS-2002 ≥ 3	1.83 (1.00, 3.36)	0.050	1.30 (0.67, 2.55)	0.440
Comorbidity (yes)	1.10 (0.58, 2.08)	0.772		
TNM stage (II-IV)	1.95 (1.02, 3.72)	0.043	1.60 (0.78, 3.25)	0.199
Pathological type (HCC)	0.56 (0.26, 1.21)	0.559		

HGS: handgrip strength; NRS-2002: Nutritional Risk Screening 2002; TNM: tumor lymph nodes metastasis stage; HCC: hepatocellular carcinoma.

Supplementary Table IV. Logistic regression of risk factors for major complications in elderly group (*n* = 85)

Variables	**Univariate**	
	OR (95 % CI)	***p*-value**
Sex (male/female)	1.13 (0.36, 3.58)	0.833
Laparotomy (yes)	4.25 (0.90, 20.06)	0.068
Extent of resection (≥ 3 segments)	2.19 (0.81, 5.95)	0.124
Intraoperative blood loss (≥ 200 ml)	2.22 (0.79, 6.20)	0.130
HGS (low)	0.80 (0.27, 2.33)	0.678
Obesity (BMI ≥ 24)	1.22 (0.47, 3.15)	0.679
NRS-2002 ≥ 3	0.77 (0.30, 1.99)	0.586
Comorbidity (yes)	0.97 (0.37, 2.54)	0.954
TNM stage (II-IV)	1.34 (0.41, 4.44)	0.630
Pathological type (HCC)	0.84 (0.26, 2.73)	0.766

HGS: handgrip strength; NRS-2002: Nutritional Risk Screening 2002; TNM: tumor lymph nodes metastasis stage; HCC: hepatocellular carcinoma.

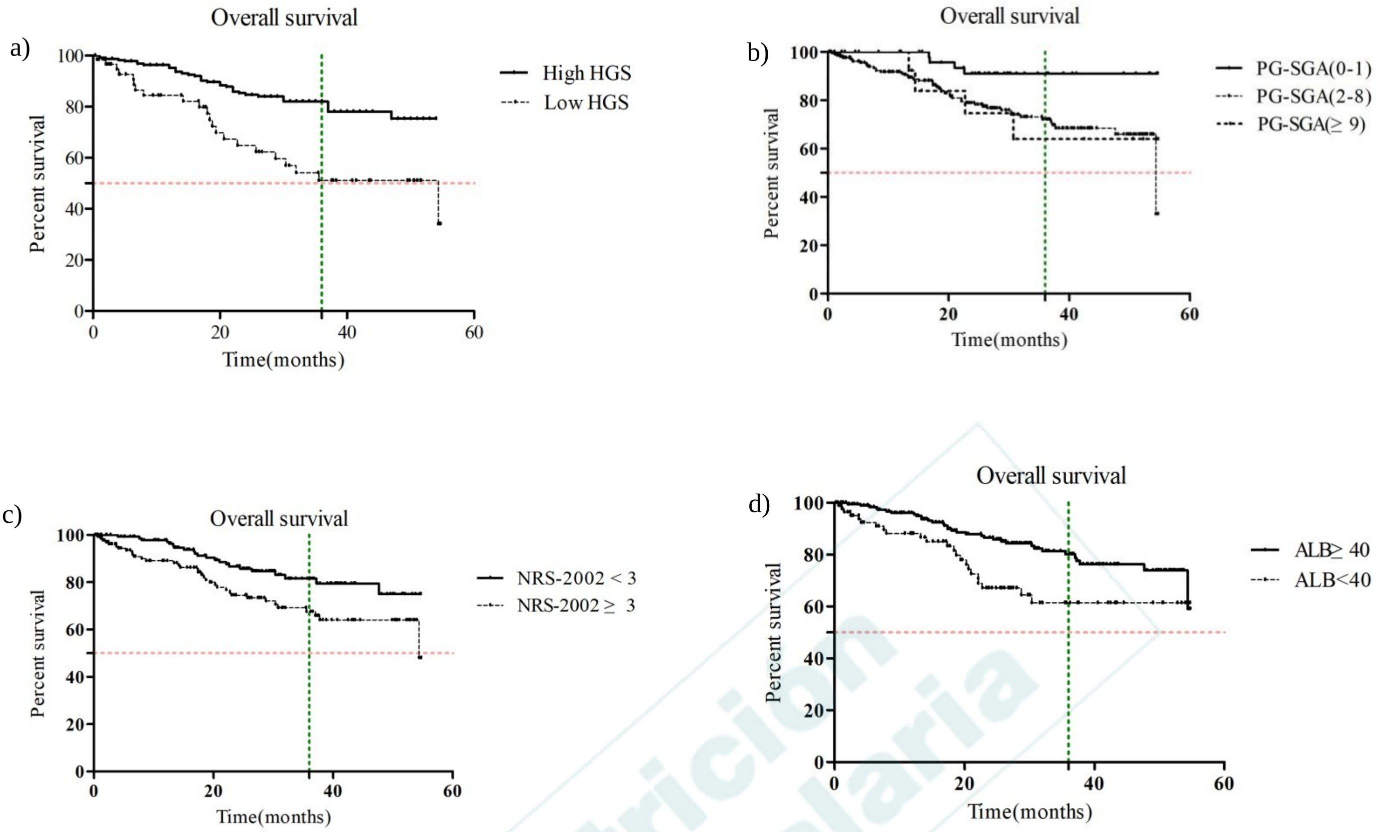

Figure 1. Kaplan-Meier curve analysis stratified by (A) HGS ($p < 0.001$), (B) PG-SGA ($p = 0.03$), (C) NRS-2002 ($p = 0.013$) and (D) ALB ($p = 0.005$). HGS: handgrip strength; PG-SGA: Patient-Generated Subjective Global Assessment; NRS-2002: Nutritional Risk Screening 2002; ALB: albumin.