Hand Grip Strength as a Predictor of Postoperative Complications Following Resection in Patients with Primary Liver Cancer: A Retrospective Cohort study

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Research

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Abstract

Background: The incidence of complications after hepatectomy for primary liver cancer (PLC) remains high. In this regard, a rapid, simple and inexpensive method is needed to assess the nutritional status of patients before surgery. This study aimed to determine the predictive value of hand grip strength (HGS) for postoperative complications of PLC.

Methods: This retrospective study was conducted at a university hospital. A total of 147 patients with PLC who underwent liver resection were enrolled. HGS was measured using an electronic hand dynamometer. According to Clavien–Dindo classification, grade 2 or higher was considered as postoperative complication. The correlations *between HGS and age/*nutritional assessment tools were analysed *using* Spearman *correlation test.* Logistic regression analysis was used to determine the risk factors for complications.

Results: About 25.2% of the patients had low HGS. The incidence rates of postoperative complications were 35.14% in the low-HGS group and 21.82% in the high-HGS group. HGS was negatively correlated with age ($P < 0.05$) in both sexes. Multivariate analysis showed that low HGS [odd ratio (OR) = 2.97, 95% CI: 1.07-8.25, $P = 0.04$] was related to postoperative complications in the total population.

Conclusion: HGS is a risk factor for postoperative complications. Additional long-term studies are needed to confirm HGS as a valuable indicator before surgery.

Introduction

Primary liver cancer (PLC) is one of the most dangerous malignancies; it ranks sixth in incidence and fourth in mortality rate among cancers worldwide. According to Globocan 2018, approximately half of new PLC cases and related death were recorded in China [(1)]. Hepatectomy is the mainstay treatment for PLC [(2)]. In recent years, the recurrence and mortality after liver resection has significantly reduced due to surgical technique advancement, rapid recovery application and perioperative management improvement. However, the postoperative complications remain at 15–50% [(3)].

Assessment of nutritional status is becoming increasingly important before surgery. A considerable amount of evidence has proven that preoperative malnutrition increases postoperative mortality [(4)] and morbidity [(5)] and reduces quality of life [(6)] and survival time [(7)]. In 1988, Halliday et al. [(8)] reported increased postoperative mortality in patients with preoperative weight loss and low albumin during hepatobiliary surgery. Nutritional risk screening 2002 (NRS-2002) score ≥ 4 [(9)] and Patient-Generated Subjective Global Assessment (PG-SGA) score ≥ 4 [(5)] are risk factors for 90-day mortality [(9)] and postoperative complications [(5)] after hepatic resection. However, a comprehensive nutritional assessment for every patient can be particularly difficult to achieve, because of the huge number of patients and limited medical resources in China. Therefore, a fast, simple and inexpensive method is needed to assess the nutritional status of patients before surgery.

Hand Grip Strength (HGS) is a validated, non-invasive and most feasible bed side method for muscle function [10], and a useful indicator in predicting nutritional level and health status [11,12]. Previous studies showed that HGS is a sensitive indicator of protein inactivation and thus can detect early changes in malnutrition [13]. A number of studies revealed that low HGS is a risk factor for postoperative complications [14,15], and increased length of hospital stay [16], treatment toxicity [17] and 6-month mortality [4] in different types of cancer.

Recent research on PLC focuses on the relationship between sarcopenia and liver resection prognosis [18,19]. The overall and recurrence-free survival rates are lower in patients with sarcopenia who underwent hepatic resection than in patients without sarcopenia [18]. However, few studies focused on the direct correlation between HGS and complications after liver resection. The present study aimed to clarify whether low HGS is a predictor of postoperative complication after hepatectomy in PLC.

Materials And Methods

Study Participants

Patients who underwent hepatic resection at Tianjin Medical University Cancer Hospital, Tianjin, China, from April 20, 2018 to Dec 31, 2019, were identified. The study inclusion criteria were as follows: ages 18 to 80 years, pathological diagnosis of primary liver cancer, well-compensated liver function (Child-Pugh A), no contraindications for surgery and no obvious hydrothorax and hydroperitoneum. The exclusion criteria were: complicated with other malignant tumors and metastatic liver cancer. The study was approved by Ethics Committee of Tianjin Medical University Cancer Hospital (No.Lx20190814).

We used a self-designed questionnaire to collect information. The data include demographic data, clinicopathological variables, nutritional statistics (NRS-2002 and PG-SGA score), preoperative laboratory test results [Albumin (ALB), prealbumin (PALB) and hemoglobin (HGB)], treatment-related data (operating time, intraoperative blood loss, type of operation and range of hepatectomy) and pathological diagnosis. Based on baseline data, all patients were staged according to the Barcelona Clinic Liver Cancer (BCLC) staging system and Child-Pugh score.

Measurement of HGS

HGS was measured using an electronic hand dynamometer (EH101; CAMRY, Guangdong, China). The measurement range was 0–99.9 kg with an accuracy of 0.1 kg. The width of the dynamometer handle was adjusted in accordance with the size of the palm to maximise grip. During the measurement, the patients were asked to stand upright with feet separated from shoulders and to keep the dynamometer away from the body. 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. Low HGS was defined as < 30 kg for men and < 20 kg for women among people ≥ 60 years as well as < 36.7 kg for men and < 20.8 kg for women aged under 60 years [20,21].

Assessment of PG-SGA

Nutritional status was evaluated using PG-SGA, which consists 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 score is divided into three levels: A (0–3) represents good nutrition, B (4–8) indicates moderate malnutrition and C (≥ 9) denotes severe malnutrition.

Assessment of NRS-2002

Nutrition risk assessment consists of three parts: disease severity score, nutritional status score and age. Given that all patient underwent liver resection, the disease severity score was 2, ranging from 2 to 6. The patients are classified as nutritionally at risk if their NRS-2002 score is at least 3 [22].

Outcomes

According to the Clavien–Dindo classification, postoperative complications of grade 2 or higher were considered as major complications [23]. Length of hospital stay was calculated as the number of days from the day of the operation to the day of discharge.

Statistical analysis

Statistical analysis was performed by SPSS 22.0 statistical software. Continuous variables were tested using Student's t-test or non-parametric Mann–Whitney U test, and categorical variables were analysed using Pearson c^2 or Fisher exact test. Correlations *betweenvariables* were analysed *using* Spearman *correlationtest*. Binomial univariate logistic regression analyses were used to evaluate the correlation between the occurrence of complications and potential risk factors. Factors with $P < 0.2$ were entered into the multivariate logistic analysis. All tests were two sided, and $P < 0.05$ was considered statistically significant.

Results

Characteristics of Participants

A total of 147 patients who underwent hepatic resection for PLC were included in this study. Among them, 114 (77.5%) were men, with mean age of 58.86 ± 9.06 years. About 25.2% (n = 37) of the patients were defined as having low HGS. Table 1 shows other basic population characteristics and the comparison of variables by HGS. The low-HGS group demonstrated significantly lower weight ($P < 0.01$), lower body mass index (BMI) ($P = 0.02$), lower albumin ($P < 0.01$) and higher PG-SGA score ($P = 0.02$) and NRS-2002 score ($P = 0.03$) than the high-HGS group.

Table 1
Sample Demographic and clinical characteristics according to handgrip strength

	ALL(n = 147)	High HGS(n = 110)	Low HGS(n = 37)	*P*
Age (years)[a]	58.86 ± 9.06	59.06 ± 8.93	58.24 ± 9.54	0.78
SEX (male)	114	85	29	0.89
Weight (kg)	68.70 ± 11.29	70.10 ± 11.64	64.51 ± 9.07	< 0.01
BMI (kg/m^2)	24.06 ± 3.13	24.40 ± 3.17	23.05 ± 2.81	0.02
PG-SGA	4.22 ± 3.09	3.89 ± 2.86	5.22 ± 3.55	0.02
NRS-2002	2.45 ± 0.91	2.37 ± 0.87	2.70 ± 0.10	0.03
ALB (g/L)	42.70 ± 3.47	43.18 ± 3.50	41.29 ± 3.01	< 0.01
PA (g/L)	0.20 ± 0.05	0.20 ± 0.05	0.20 ± 0.05	0.97
HGB (g/L)	147.73 ± 14.22	148.45 ± 13.64	145.59 ± 15.82	0.29
laparoscope (Minimal invasive approach)	32	22	10	0.37
Intraoperative blood loss (mL) ≥ 200	55	45	10	0.13
Extent of operation Complex (≥ 3 segments)	51	40	11	0.46
BCLC stage				
0	1	0	1	0.28
A	57	42	15	
B	78	58	20	
C	11	10	1	
operation time(min)	157.97 ± 62.60	153.91 ± 50.20	171.83 ± 93.27	0.90
Postoperative hospital stay (day)	10.59 ± 5.87	10.08 ± 4.78	12.08 ± 8.22	0.36
HGS (kg)	34.76 ± 9.66	37.16 ± 9.30	27.65 ± 6.85	< 0.01
Postoperative complications	37	24	13	0.11

	ALL(n = 147)	High HGS(n = 110)	Low HGS(n = 37)	*P*
Histopathological type				
HCC	123	90	33	0.04
ICC	18	17	1	
cHCC-CC	6	3	3	

BMI: Body Mass Index; ALB: Albumin; PA: prealbumin; HGB: Hemoglobin; HGS: hand grip strength; HCC: Hepatocellular Carcinoma; ICC: Intrahepatic Cholangiocarcinoma; cHCC-CC: Combined hepatocellular carcinoma and cholangiocarcinoma;

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.

Correlation Between Hgs And Age

The correlation between HGS and age was analysed using Spearman correlation test. Figure 1 shows that HGS was negatively correlated with age in all patients (male: −0.403, $P < 0.001$; female: −0.362, $P = 0.039$).

Correlation Between Hgs And Other Nutritional Assessments

The relationship between HGS and nutritional assessment tools was analysed by gender (Table 2). In males, HGS was weakly correlated with BMI/ ALB/ PA and negatively correlated with NRS-2002 score. In females, HGS was negatively correlated with PG-SGA scores (r = − 0.390, $P = 0.025$).

Table 2
Correlation between grip strength and nutritional assessment methods

	male(n = 114)		female(n = 33)	
	r	*P*	r	*P*
PG-SGA	-0.103	0.274	-0.390	0.025
BMI	0.338	0.001	0.167	0.352
ALB	0.229	0.014	-0.066	0.716
PA	0.193	0.046	0.052	0.773
NRS-2002	-0.192	0.041	-0.244	0.171

Postoperative Complications Graded By Clavien–dindo Classification And Outcomes

In accordance with the Clavien–Dindo Classification (Table 3), 37 patients (25.17%) exhibited grade 2 postoperative complications. The incidence of postoperative complications was higher in the low-HGS group than in the high-HGS group (35.14% versus 21.82%), but the difference was not statistically significant ($P = 0.11$).

Table 3
Postoperative complications (Clavien–Dindo classification)

Grade	Total	Low HGS (*n* = 37)	High HGS (*n* = 110)	*P*
Total, n(%)	37(25.17)	13(35.14)	24(21.82)	0.11
Grade 2	23	7	16	0.21
Grade 3a	7	2	5	
Grade 3b	3	1	2	
Grade 4a	3	2	1	
Grade 4b	1	1	0	
Grade 5	0	0	0	

Univariate And Multivariate Analyses Of Postoperative Complications

As shown in Table 4, univariate analysis showed that postoperative complications were significantly related to laparotomy ($P = 0.03$), extent of surgical complexity (≥ 3 segments) ($P < 0.01$) and blood loss (≥ 200 ml) ($P < 0.01$). Low HGS, Obesity (BMI ≥ 28), ALB ≤ 40 and PG-SGA ≥ 9 showed a P value of lower than 0.2. Multivariate analysis revealed that low HGS [odd ratio (OR) = 2.97, 95% confidence interval (CI): 1.07–8.25, $P = 0.04$], laparotomy (OR = 4.06, 95% CI: 1.16–14.22, $P = 0.03$) and blood loss ≥ 200 (OR = 4.52, 95% CI: 1.94–11.44, $P < 0.01$) were independently related to postoperative complications.

Table 4
Logistic regression of risk factors for complications

variables	**Univariate**		**Multivariate**	
	OR(95%CI)	***P***	**OR(95%CI)**	***P***
sex(1 = famle)	0.94(0.38–2.31)	0.89		
Age(≥ 60)	0.85(0.40–1.79)	0.67		
laparotomy(yes)	4.06 (1.16–14.22)	0.03	4.93(1.21–20.13)	**0.03**
Extent of operation Complex (≥ 3 segments)	3.00(1.39–6.47)	0.01	2.34(0.98–5.56)	0.06
Intraoperative blood loss (≥ 200 ml)	4.00(1.83–8.75)	0.01	4.52(1.94–11.44)	**0.01**
HGS(LOW)	1.94(0.86–4.37)	0.11	2.97(1.07–8.25)	**0.04**
Obesity(BMI ≥ 28)	2.17(0.72–6.58)	0.17	2.62(0.73–9.44)	0.14
ALB(≤ 40)	2.03(0.88–4.70)	0.10	1.74(0.64–4.73)	0.28
PA(≤ 0.2)	1.40(0.64–3.07)	0.40		
PG-SGA(≥ 9)	2.17(0.72–6.58)	0.17	1.81(0.49–6.68)	0.38
NRS ≥ 3	1.19(0.55–2.55)	0.66		

Discussion

This study aimed to explore the relationship between HGS and postoperative complications of PLC. Low HGS, laparotomy and intraoperative blood loss (≥ 200 ml) were significant risk factors for complications after surgery. The results also revealed a certain correlation between HGS and other nutrition assessment tools. This clinical study is the first to assess the relationship between HGS and short-term surgical outcomes after hepatic resection in patients with PLC.

HGS is an indicator of overall muscle strength and reflects physical function [11]. Few studies have focused on the relationship between preoperative HGS and prognosis in PLC, while a number of works

have investigated gastric [24], pancreatic [25] and esophageal cancer [14]. Sato et al. [14] reported that HGS is a predictor of postoperative complications, especially postoperative pneumonia in men aged 70 years or older; however, no correlation was found in patients younger than 70. According to Sato et al. [26], preoperative HGS rather than lean body mass is a risk factor for postoperative complications. Therefore, HGS has become a popular indicator in basic assessment for clinical applications.

Sarcopenia is defined by the new edition of European Working Group on Sarcopenia in Older People as a decline in gait speed, HGS and muscle mass [27]. Many studies have focused on the association between sarcopenia and short- [18] and long-term prognosis after hepatectomy in patients with liver cancer. Harimoto N et al.[18,19] reported that sarcopenia is one of the 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 [28], but complications were not analysed as key outcome variables in this study. Findings from Europe and America reached a slightly different conclusion. A study conducted by Valero et al. [29] reported that severe complications (Clavien grade ≥ 3) occur 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, sarcopenia was not assessed in our study. Several components of sarcopenia such as muscle quantity or gait speed were not included in our study. However, sarcopenia is rarely used in clinical practice due to factors, such as economic and operational complexities.

In this study, the incidence of grade 2 or higher complications was 25.2%, which is similar to that in a previous research (29%) [28]. To our knowledge, surgical complications are poor prognostic factors after surgery for hepatocellular carcinoma (HCC) [18]. Yang et al. [30] showed that the short-term postoperative complications of HCC affect the overall postoperative and recurrence-free survival. Medical teams always strive to reduce the incidence of complications. In addition, surgical blood loss (≥ 200 ml) was identified as an independent risk factor for complications. Intraoperative bleeding was used to predict treatment outcomes [31], mortality and recurrence [32].

Low HGS was significantly associated with low weight, low BMI, low albumin, high NRS-2002 and high PG-SGA score in baseline analysis. Further analysis found a significant correlation between HGS and nutritional assessment tools, such as PG-SGA ($r = -0.390$, $P = 0.025$) in women. Previous studies debated whether HGS reflects nutritional status [33]. These results are consistent with reports among elderly hospitalised patients. Hence, patients with high HGS have a low risk of malnutrition and nutritional risk [34]. Furthermore, changes in HGS can independently predict changes in PG-SGA scores over a period of time [12].

In the final multivariate analysis, other nutritional assessment methods such as PG-SGA, NRS-2002, ALB/PALB and BMI were no longer meaningful in predicting postoperative complications. The results are inconsistent with those of a previous research [5], where PG-SGA scores ≥ 4 were considered as

significant risk factors for postoperative complications. The following points may explain the differences. Firstly, malnutrition and low HGS do not entirely appear simultaneously [33]. Further research is needed to determine which comes first. Secondly, existing nutritional assessment tools may lack sensitivity to subtle changes in liver cancer before surgery. Thirdly, in the present study, the enhanced recovery protocol after surgery was applied, which possibly improve the patients' postoperative condition and eliminate the consequences of malnutrition. Nevertheless, muscle function responds to early nutritional deprivation and recovery [10]. In the present work, we showed that HGS is a simple tool that can be used to monitor nutritional status. HGS may detect body changes earlier than current anthropometric-based screening tools.

Clinical practice guidelines recommend that patients with liver disease should be evaluated for malnutrition and sarcopenia before surgery. With proper sarcopenia treatment, the body's protein status and clinical outcomes can be improved [35]. Furthermore, improving muscle condition with nutritional supplements and physical exercise can affect postoperative outcomes [36].

One advantage of this study is that HGS and nutrition were assessed by the same trained dietitian, thereby avoiding differences between evaluators. In addition, various preoperative nutritional assessment tools were used to comprehensively assess the patients' overall preoperative status. Nevertheless, this study has some limitations. Firstly, long-term data and survival information were not available. We will continue to track the health status of these patients over time. Secondly, the sample size was too small to discuss the optimal truncation value by gender and age. To identify patients at risk, researchers must verify reliable cut-off values in the future. Thirdly, the study was only conducted in one centre and thus could not represent other regions or races. Additional cohort studies are needed to analyse the relationship between HGS and long-term outcomes.

Conclusions

Preoperative HGS exerts negative effects on postoperative complications after liver surgery in patients with PLC. HGS is a simple and inexpensive indication of nutritional status among surgical patients. We suggest the use of HGS as a routine measure before surgery because any staff can operate grips in accordance with the prescribed procedures.

Declarations

Ethics approval and consent to participate

The study was approved by Ethics Committee of Tianjin Medical University Cancer Hospital (No. Lx20190814).

Consent for publication

All presentations of case are approved for publication.

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests, funding and authors' contributions

None of the authors have any conflict of interest in presenting this work.

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Song Tianqiang contributed to conceiving, coordinating and design the study. Li Chunlei participated in the design of the study, data analysis and writing the manuscript. Zeng Yaqi, Chen Yajun and Wang Yujie contributed to data discrimination and data collection. Wu Hongmei contributed to making plots and the revision of the manuscript. All authors have critically reviewed the final version of the manuscript and agree to publish it.

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Figures

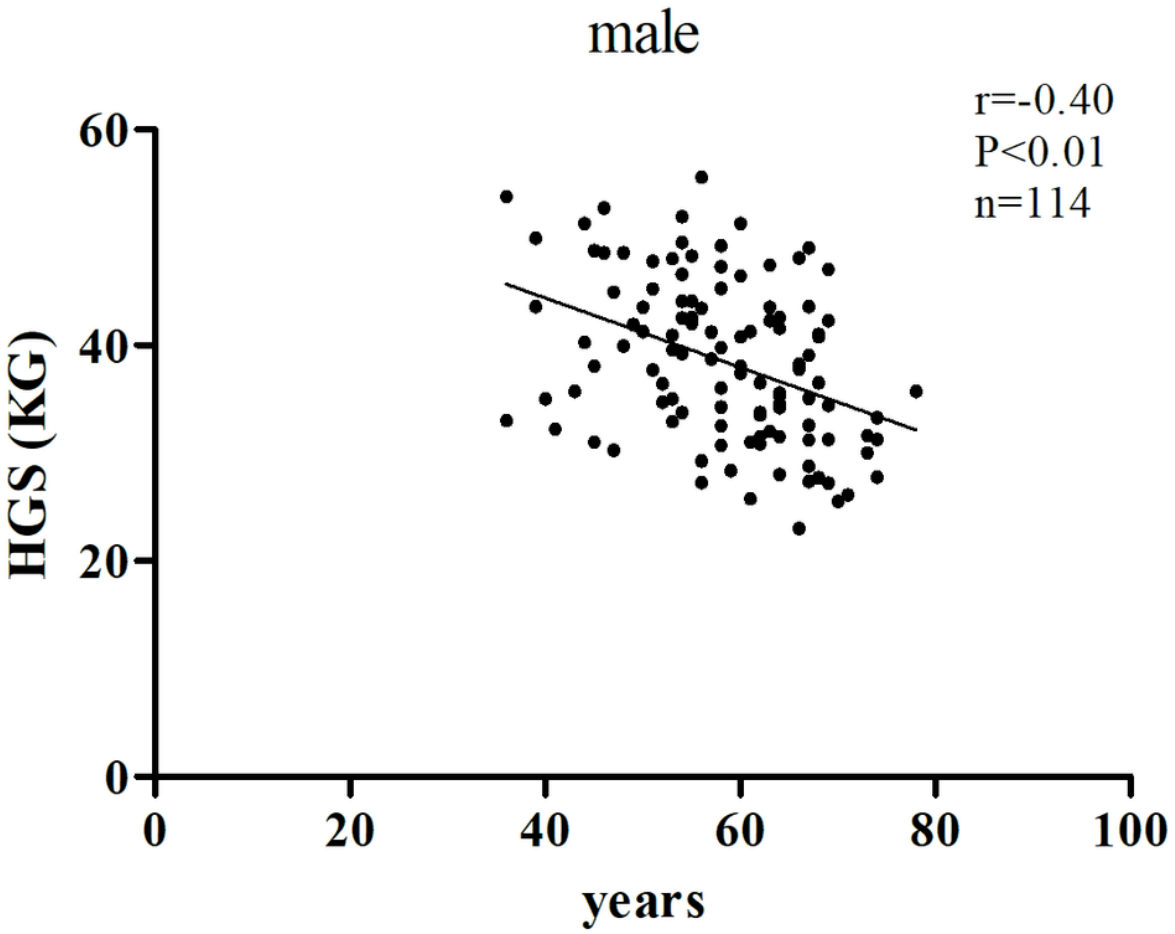

Figure1. The relationship between age and grip strength in male

Figure 1

The relationship between age and grip strength in male

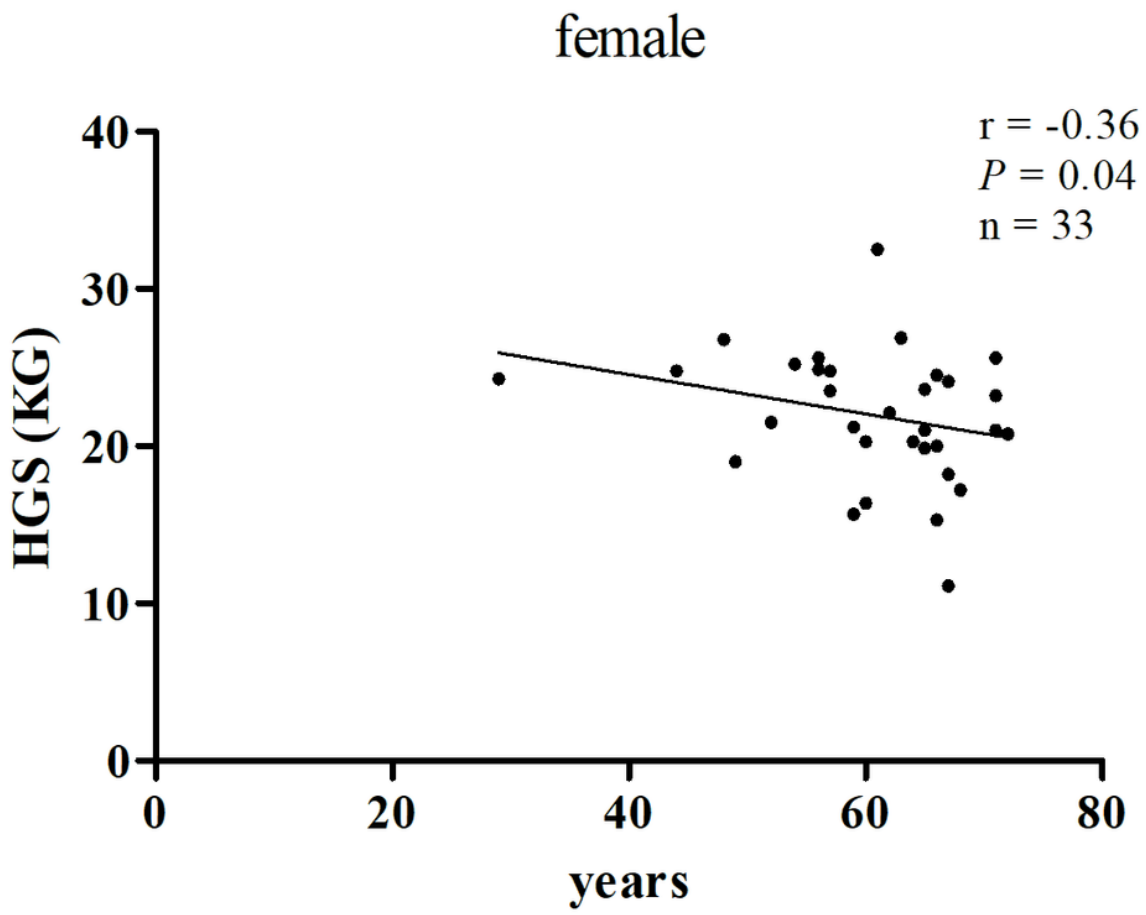

Figure2. The relationship between age and grip strength in female

Figure 2

The relationship between age and grip strength in female