



Handgrip Strength and Mortality in Maintenance Hemodialysis Patients

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Abstract

Background: Muscle strength assessment is a convenient clinical test that has shown to correlate with the nutritional status of dialysis patients. Articles written in English to investigate the association between Handgrip Strength (HGS) and mortality in Maintenance Hemodialysis (MHD) patients are mainly from Brazil and several other non-Asian countries.

Objectives: This study aimed to examine the association of HGS with all-cause mortality in Chinese MHD patients.

Methods: The current multicenter observational longitudinal study enrolled MHD patients from June 2015 to June 2016. The study setting was seven dialysis centers of tertiary general hospitals in Guizhou province, China. Patients were followed up until June 2018. The ROC curves were plotted to seek the best cutoffs for HGS to predict mortality in men and women. Survival analysis was done using the Kaplan-Meier survival curve and the Cox proportional hazard model.

Results: We enrolled 857 MHD patients and followed up for 24.9 ± 10.2 months. During the follow-up, 204 (23.8%) patients died, 39 (4.6%) received renal transplantation, 18 (2.1%) switched to peritoneal dialysis, and 118 (11.7%) were transferred to nonparticipating dialysis units. The cutoff value of HGS to predict all-cause mortality was 12.4 kg for women and 25 kg for men. Utilizing the cutoffs to fit the survival curve of Kaplan-Meier, the correlation of HGS with mortality was verified for both genders. After adjustment for demographic and biochemical variables, HGS remained an independent predictor of all-cause mortality.

Conclusions: Handgrip strength was strongly associated with all-cause mortality in patients receiving MHD. The cutoff values to predict all-cause mortality were 12.4 kg for women and 25 kg for men. Handgrip strength may be incorporated into clinical practice for assessing functional status and predicting prognosis in MHD patients.

Keywords: Hand Strength, Protein-Energy Malnutrition, Mortality, Renal Dialysis

1. Background

Chronic Kidney Disease (CKD) has emerged as a global public health burden. Individuals with CKD experience high cardiovascular and all-cause mortality rates. Protein-Energy Malnutrition, now named Protein-Energy Wasting (PEW), featured by the reduction of visceral protein stores and the loss of body mass and muscle mass is one of the major CKD complications (1). According to different diagnostic criteria, the incidence of PEW in hemodialysis patients of CKD stage 5 varies from approximately 23% to 76% (2). Because PEW is closely related to the unacceptably high morbidity and death risk in patients with Maintenance Hemodialysis (MHD), the frequent evaluation of PEW and resistance exercises are recommended for preventing malnutrition and improving survival (1, 3, 4). Although the current diagnostic criteria of PEW, such as the International Society of Renal Nutrition and Metabolism (ISRNM) crite-

ria, Subjective Global Assessment (SGA), or Malnutrition-inflammation Score (MIS), can predict outcomes in MHD patients, their uses are time-consuming and require specialized knowledge in renal nutrition for an accurate evaluation. Handgrip Strength (HGS), one of the criteria used to define sarcopenia (5), has demonstrated to be a simple, non-invasive, and reliable indicator that reflects nutrition status and muscle function in studies of CKD patients and the general population (6-8). Handgrip strength can be utilized as a convenient nutritional test to recognize dialysis patients with a higher possibility of PEW. It seems to not be influenced by hydration status like other methods for lean body mass evaluation (7, 9-11). So far, several studies have reported a negative relationship between HGS and mortality risk mainly in non-Asian hemodialysis patients (12-16). However, some studies failed to show a statistically significant association between HGS and all-cause mortality (17,

18). Moreover, only three studies in Brazil gave a clear HGS cutoff predicting this poor outcome in a specific population (14-16).

2. Objectives

The present study was conducted to determine the HGS cutoff values for both genders and examine its relationship with all-cause mortality among Chinese MHD patients.

3. Methods

3.1. Participants and Study Designs

The current multicenter observational longitudinal study included MHD patients from seven dialysis centers of tertiary general hospitals in Guizhou province, China, from June 2015 to June 2016. Eligible participants were over 18 years of age, receiving hemodialysis three times a week for at least three months. The exclusion criteria included the absence of nutritional assessment data and unwillingness to participate. The survival rate was assumed to be 80% and the Area Under the Curve (AUC) was expected to be at least 0.65. With a power of 90% and α of 0.05, the sample size was estimated at 245. The final study population consisted of 857 HD patients (Figure 1). The MHD patients were followed up until kidney transplant, a change to peritoneal dialysis, transfer to a nonparticipant dialysis center, death, or until the end of the follow-up in June 2018.

3.2. Clinical Assessments and Data Collection

One researcher examined the participants and others collected recent, relevant laboratory and clinical data from medical records. Anthropometric measurements were obtained from a nutritional assessment performed before the start of the dialysis session. Height, body weight, calf circumference, and mid-arm circumference were measured. Using CAMRY® dynamometer with a precision of 0.1 kg, HGS was measured in the dominant or non-fistula hand. The patients sitting with their arms bent at an angle of 90° on a horizontal level held the tool with the fingers around it. Three measures were taken with 30 seconds of rest between each test and the maximum score was adopted for the study.

3.3. Statistical Analyses

Continuous data with a normal distribution were expressed as means \pm SD and compared by the Student's *t* test. Continuous data without normal distribution were expressed as medians and interquartile ranges and compared by the Mann-Whitney U test. Categorical data were expressed as frequencies and percentages and compared by the chi-square test. Nonparametric ROC curves were

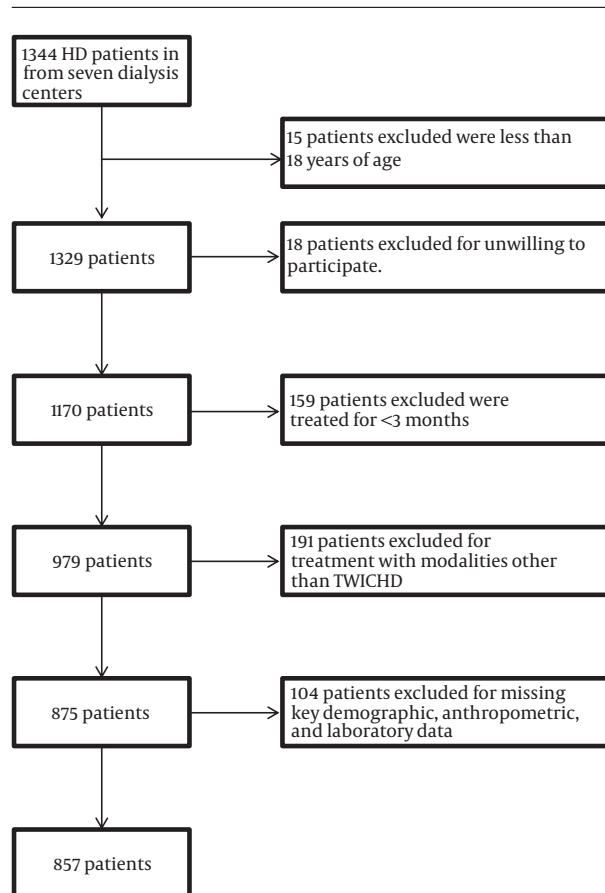


Figure 1. The flow chart of study participants. TWICHD, thrice-weekly in-center HD.

plotted to seek the best cutoffs for HGS to predict mortality in men and women. Survival analysis was done using the Kaplan-Meier survival curve. The proportional hazards assumptions were checked before using the Cox proportional hazard model to analyze the association of HGS with mortality. Plausible demographic and biochemical confounders were incorporated as multivariable covariates in the analysis of the correlation between HGS and mortality. Handgrip strength was incorporated into Cox regression analysis as a continuous variable or categorical variable according to the cutoff values for men and women. Statistical analysis was carried out using SPSS software, version 19.0 (SPSS Inc, Chicago). A P value of < 0.05 was considered statistically significant.

3.4. Ethical Statement

The procedures of the study were explained to all participants. Based on the Declaration of Helsinki, medical ethics was considered in this study and the participants were reassured that their individual information would

be kept confidential. Written informed consent was taken from all participants.

4. Results

4.1. Characteristics of Participants

The baseline characteristics are shown in [Table 1](#) for the whole study population, men, and women. The study enrolled 857 patients (507 men and 350 women) who had been receiving MHD treatment for more than three months. The major cause of CKD was chronic glomerulonephritis in 488 (56.9%) patients, diabetic kidney disease in 240 (28.0%) patients, and hypertensive nephropathy in 77 (9%) patients. None of the MHD patients had active hand arthritis at the time of HGS evaluation. The median HGS of all patients was 20.4 kg. The median HGS was 25.1 kg for men and 15.1 kg for women ($P < 0.001$).

4.2. Follow-up

After being followed up for a mean duration of 24.9 ± 10.2 months (minimum 3 and maximum 36 months), 204 patients (117 men and 87 women, 23.8%) died, 39 patients (4.6%) underwent kidney transplantation, 18 (2.1%) patients changed to peritoneal dialysis, and 118 (11.7%) patients were transferred to nonparticipating dialysis units.

4.3. ROC Curve

According to the nonparametric ROC curves for men, the optimized cutoff point for HGS to predict death was 25 kg, with a sensitivity of 72% and specificity of 57% (AUC 0.674; 95% CI 0.621 - 0.727; $P < 0.0001$) ([Figure 2A](#)). The positive and negative predictive values were 33.4% and 87.1%, respectively. The positive and negative likelihood ratios were 1.674 and 0.491, respectively. For women, the best cutoff point for HGS to predict death was 12.4 kg with a sensitivity of 54% and specificity of 72% (AUC 0.673; 95% CI 0.607 - 0.739; $P < 0.001$) ([Figure 2B](#)). The positive and negative predictive values were 38.9% and 82.6%, respectively. The positive and negative likelihood ratios were 1.929 and 0.639, respectively.

4.4. Kaplan-Meier Survival Analysis

The association of HGS with all-cause mortality for both men and women was verified by the survival probability analysis ([Figure 3](#)). The results indicated the statistical significance for both men ($\chi^2 = 34.347$, $P < 0.0001$) ([Figure 3A](#)) and women ($\chi^2 = 23.383$, $P < 0.0001$) ([Figure 3B](#)).

4.5. Cox Proportional Hazards Analysis

The Cox regression analysis results of the relationship between HGS and all-cause mortality are summarized in [Table 2](#). Crude analysis showed that HGS was a significant predictor of mortality. In the model adjusted for all the included covariates, higher HGS levels remained closely associated with a lower hazard of death.

5. Discussion

Similar to other reports on dialysis patients, the present study showed that HGS median values in both men and women were significantly lower than the references described for the healthy population ([6](#), [14](#), [15](#), [19](#)). It was reported that the muscle strength of HD patients could be less than 50% of that in healthy participants ([20](#), [21](#)). Uremia complications and dialysis procedure itself may be related to lower values of HGS ([7](#), [8](#), [22](#)). Therefore, the HGS cutoff points based on the general population to predict malnutrition, clinical complications, or even poor prognosis are not appropriate for MHD patients. Moreover, there are also racial differences in muscle mass and strength and different populations should have their own HGS cutoff values to define weakness. In patients undergoing MHD, dialysis therapy may lead to hypotension and a poor general condition, negatively affecting HGS measurement after the dialysis session ([23](#), [24](#)). Therefore, it should theoretically be performed before dialysis sessions. However, Leal et al. found that HGS values were not different before and after HD ([11](#)).

This study showed an independent association between HGS and all-cause mortality in both men and women, even after adjustment for both CRP and albumin. Other similar studies did not correct for these two indicators at the same time ([12-18](#)). In addition, compared to other studies with non-Asian MHD patients, we analyzed the association between all-cause mortality and HGS with both categories and continuous values of HGS. Other study strengths are the relatively large sample size and complete data collection of all variables needed in the analysis. When predictive values and likelihood ratios were considered, the HGS value of exclusion diagnosis seemed to be greater. Some studies suggested that muscle strength may be a better predictor of outcomes than the lean tissue mass in hemodialysis patients ([12](#), [13](#), [25](#)). According to the most recent version of the European Working Group on Sarcopenia in Older People, the muscle strength measurement is highlighted while muscle mass assessment is used to confirm the diagnosis ([5](#)). Recently, Valenzuela et al. found that HGS appeared to be a better and more practical predictor of mortality than plasma biomarker S-klotho in male dialysis patients ([26](#)). Therapeutic measures for targeting

Table 1. Baseline Demographic and Biochemical Characteristics of the Patients^a

Characteristics	Total (N = 857)	Men (N = 507)	Women (N = 350)	P Values
Age, y	55 ± 16	55 ± 16	55 ± 16	0.996
Diabetes	260 (30.3)	164 (32.2)	96 (27.4)	0.131
CVD	353 (41.2)	217 (42.8)	136 (38.9)	0.259
Follow-up, mo	24.6 ± 10.4	24.4 ± 10.4	25.0 ± 10.3	0.403
Dialysis vintage, y	2.5 (1.1 - 3.9)	2.6 (1.1 - 4.0)	2.4 (1.0 - 3.9)	0.796
BMI, kg/m ²	23.2 ± 3.5	23.2 ± 3.2	23.3 ± 3.8	0.864
MAC, cm	24.9 ± 3.0	25.1 ± 2.8	24.7 ± 3.4	0.121
CC, cm	32.2 ± 3.3	32.8 ± 3.1	31.3 ± 3.3	0.000
HGS, Kg	20.4 (14.3 - 27.4)	25.1 (18.7 - 31.2)	15.1 (11.4 - 19.8)	0.000
SBP, mmHg	140 ± 21	141 ± 21	138 ± 21	0.032
DBP, mmHg	77 ± 14	77 ± 14	76 ± 14	0.431
White blood cell, 1000/mm ³	6.1 (4.9 - 7.3)	6.1 (5.0 - 7.5)	5.9 (4.8 - 7.2)	0.124
Hemoglobin, g/L	104 ± 20	106 ± 20	100 ± 19	0.000
Albumin, g/L	39.4 (36.0 - 42.3)	39.7 (36.0 - 42.4)	39.1 (35.8 - 41.9)	0.120
BUN, mmol/L	20.2 ± 8.0	20.8 ± 7.9	19.3 ± 8.0	0.007
Creatinine, μmol/L	854 ± 320	920 ± 335	756 ± 265	0.000
Uric acid, μmol/L	412 ± 118	416 ± 117	406 ± 118	0.199
Total cholesterol, mmol/L	3.8 ± 1.1	3.7 ± 1.1	4.0 ± 1.1	0.001
Triglyceride, mmol/L	1.5 (1.0 - 2.0)	1.3 (0.9 - 2.0)	1.7 (1.1 - 2.5)	0.000
LDL-c, mmol/L	2.3 ± 0.9	2.2 ± 0.8	2.3 ± 1.1	0.101
HDL-c, mmol/L	1.2 ± 0.5	1.1 ± 0.4	1.2 ± 0.5	0.011
Calcium, mmol/L	2.1 ± 0.3	2.1 ± 0.3	2.2 ± 0.3	0.063
Phosphate, mmol/L	1.7 ± 0.6	1.7 ± 0.6	1.7 ± 0.6	0.026
Magnesium, mmol/L	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.3	0.973
iPTH, ng/L	326 (183 - 619)	322 (188 - 596)	331 (165 - 658)	0.855
CRP, mg/L	3.0 (1.0 - 9.0)	3.6 (1.1 - 10.0)	3.7 (1.0 - 7.4)	0.024

Abbreviations: BMI, Body Mass Index; BUN, Blood Urea Nitrogen; CC, Calf Circumference; CRP, C-reactive Protein; CVD, Cardiovascular Disease; DBP, Diastolic Blood Pressure; HDL-c, High-density Lipoprotein Cholesterol; HGS, Handgrip Strength; iPTH, Intact Parathyroid Hormone; LDL-c, Low-density Lipoprotein Cholesterol; MAC, mid-arm Circumference; SBP, Systolic Blood Pressure.

^aData are presented as mean ± SD, No. (%) and median (25th - 75th).

Table 2. Univariate and Multivariate Cox Regression Hazard Ratios for the Association Between HGS and All-cause Mortality in MHD Patients^a

Covariate Type	Unadjusted				Adjusted Model 1 ^b				Adjusted Model 2 ^b			
	HR (95% CI)	B	SE	P	HR (95% CI)	B	SE	P	HR (95% CI)	B	SE	P
Continuous variable	0.939 (0.921 - 0.956)	-0.063	0.009	0.000	0.960 (0.938 - 0.983)	-0.040	0.012	0.001	0.964 (0.941 - 0.987)	-0.037	0.012	0.003
Dichotomous variable (Higher vs. Lower)	0.358 (0.269 - 0.476)	-1.028	0.145	0.000	0.653 (0.480 - 0.890)	-0.426	0.158	0.007	0.690 (0.502 - 0.948)	-0.371	0.162	0.022

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval.

^aAccording to the cutoffs for each gender, HGS is a categorical variable.

^bAdjusted model 1 included age, gender (when HGS as continuous variable), diabetes mellitus, cardiovascular disease, and dialysis vintage; Adjusted model 2 included calf circumference, albumin, C-reactive protein, and hemoglobin in addition to covariables in adjusted model 1.

both muscle mass stores and muscle strength, such as anabolic agents and amino acid supplements combined with endurance exercise, are probable to bring the best efficacy for MHD patients (27).

Despite the predictability of the HGS measurement, it has not been routinely assessed and is not always available in dialysis patients. A few studies targeting hemodialysis populations have shown HSG cutoff points to predict mor-

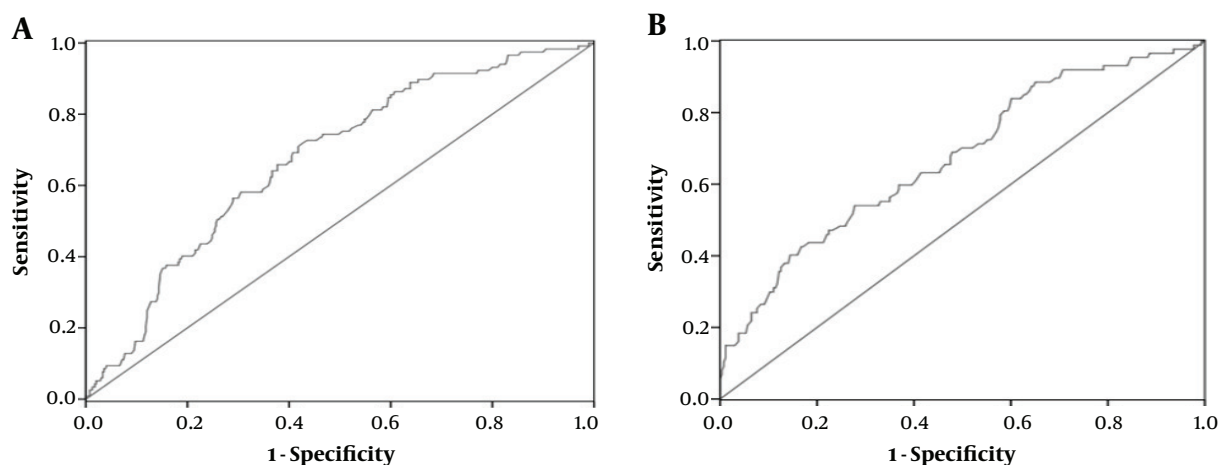


Figure 2. ROC curves showing the prediction value of all-cause mortality by HGS for men (A) and women (B)

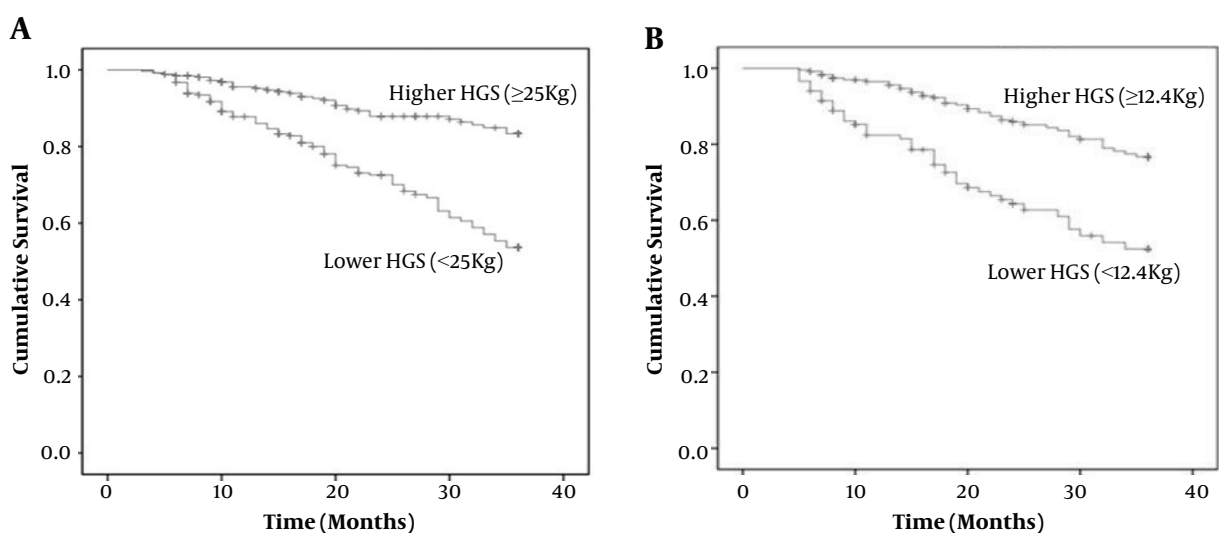


Figure 3. Kaplan-Meier survival analysis of HGS for men (A) and women (B)

tality. Matos et al. demonstrated that cutoffs of 21.5 kg for women and 28.3 kg for men could best predict this poor outcome in patients with hemodialysis (14). Also, in HD patients from Brazil, Vogt et al. showed that cutoff points predicting all-cause mortality were 22.5 kg in men and 7 kg in women (15). In this study, the best cutoffs were 25 kg and 12.4 kg, respectively. Different studies reported different cutoff values for HGS. Therefore, this study could not provide an absolute cutoff value to be applied in clinical practice.

Some limitations of the study should be considered. Longitudinal changes in HGS measurements were not evaluated during follow-ups. As an observational study, it is im-

possible

to exclude the possibility that the results were influenced by nonmeasured confounding factors. Some studies have suggested that weak HGS is an important predictor of cardiovascular events in both MHD patients and the general population (28-30). However, we could not examine the relationship between HGS and disease-specific mortality, especially cardiovascular disease, because the exact causes of death were lacking.

5.1. Conclusions

Handgrip strength is regarded as an independent predictor of mortality in Chinese MHD patients, with different

cutoffs for genders. The HGS measurement can be used as a simple and reliable tool in clinical practice to assess the nutrition status and predict the prognosis of MHD patients, especially when a dietician is not available such as in areas with limited medical resources.

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Footnotes

Authors' Contribution: Qian Li conducted anthropometric measurements. Maolu Tian and Jing Yuan analyzed the data. Maolu Tian drafted the manuscript. Maolu Tian, Yan Zha, and Jing Yuan discussed the results of the manuscript. Yan Zha revised the manuscript and edited the language. All authors read and approved the final manuscript.

Conflict of Interests: The authors declare they have no conflicts of interest.

Ethical Approval: This study scheme was approved by the Ethics Committee of participating hospitals (Code: Lunshenzi[2015]29; Date: 2015/04/10).

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