

# Hand Grip Strength is Inversely Associated with Albumin to Creatinine Ratio Among Type 2 Diabetes Patients in a Community-Based Study

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## Research Article

**Keywords:** hand grip strength, albumin to creatinine ratio, type 2 diabetes

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# **Hand grip strength is inversely associated with albumin to creatinine ratio among Type 2 Diabetes patients in a community-based study**

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**Key Words: hand grip strength; albumin to creatinine ratio; type 2 diabetes**

## **Abstract**

**Aims:** The relationship of albuminuria with hand grip strength in patients with type 2 diabetes was still uncertain. We carried out a cross-sectional study to examine the association between serum hand grip strength and albumin to creatinine ratio (ACR) among Chinese patients with Type 2 Diabetes in a community-based study.

**Methods:** A total of 427 Chinese type 2 diabetic patients were recruited from five clinical centers from March to May in 2019. Anthropometry indicators, hand grip strength, biochemical parameters and indices of glucose metabolism were measured. ACR was categorized as normo- (ACR<30 mg/g) and albuminuria (ACR≥30 mg/g). Both anthropometry and biochemical measurements were compared between these two groups categorized by ACR levels. Binary logistic regression analyses were carried out to evaluate the association of albuminuria and other clinical or biochemical variables. The correlation between hand grip strength and log(ACR) was examined by Pearson's correlation analyses. P values<0.05 were considered statistically significant for all analyses.

**Results:** Age, HbA1c, FPG, TG, Scr and SBP were all higher in correlation with higher levels of ACR, while hand grip strength was the reverse. Binary logistic regression analyses showed that high hand grip strength was an independent protective factor of the presence of albuminuria.

**Conclusions:** High hand grip strength might have a protective role in the progression of type 2 diabetic nephropathy.

## **1. Introduction**

With the prevalence of diabetes increases year by year, the incidence and prevalence of diabetic nephropathy (DN) have grown significantly all over the world. DN is one of the most severe microvascular complications of diabetes and the largest single cause of end-stage renal disease (ESRD), affecting millions of people.<sup>1</sup> Since DN is usually strongly related to cardiovascular diseases as well as ESRD, annual medical costs paid for DN are awfully high.<sup>2</sup> If not detected at early stage of the disease, the rate of morbidity and mortality would rise significantly. Therefore, early diagnosis and prevention are both essential. Urinary albumin-to-creatinine ratio (ACR) is an important component to predict renal dysfunction, which is widely used as a first clinical signal of the presence of DN.<sup>3-4</sup>

Diabetic patients showed a greater decline in muscle mass and muscular strength.<sup>5</sup> Hand grip strength, as a proxy for muscular strength, was associated with various health outcomes. A prospective population based study suggested grip strength was strongly and inversely associated with all cause mortality and incidence of and mortality from cardiovascular disease (CVD), respiratory disease and nearly all cancers.<sup>6</sup> Another prospective, general population cohort study showed that the risk of all-cause mortality

and CVD incidence and mortality is lower in people with a higher grip strength, both with and without diabetes.<sup>7</sup> Hand strength was also reported to be impaired in individuals with diabetic peripheral neuropathy.<sup>8</sup> The Concord Health and Ageing in Men Project (CHAMP) study found that participants with mild-to-moderate renal impairment had a greater decline in hand grip strength compared to those with normal renal function.<sup>9</sup> However, the relationship between hand grip strength with diabetic neuropathy, one of the diabetic complications, remains to be established.

To further assess the relation of hand grip strength and ACR, we now carried out a cross-sectional study to examine the association between hand grip strength and ACR among Chinese patients with Type 2 Diabetes Mellitus(T2DM). We hypothesized that hand grip strength may be inversely associated with ACR in Chinese patients with T2DM.

## **2. Materials and Methods**

### **2.1. Study population and design**

This was a cross-sectional, community-based study conducted from March 2019 to May 2019 including a total of 427 adults aged 35–91 years with T2DM. Entry criteria included willingness to participate in the study, diagnosis of Type 2 Diabetes. Exclusion criteria included breast feeding or pregnant women, patients with renal function rapidly changed and urinary tract infection.

The study was approved by the Human Investigation Ethics Committee at Huashan Hospital, which conforms to the provision of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013). Written informed consent was obtained from all participants prior to commencing the study.

### **2.2. Clinical Evaluation**

A comprehensive medical examination, including medical history, physical examination, resting blood pressure and heart rate was performed on each study subject. Height was measured to the nearest 0.1 cm and body weight to the nearest 0.1 kg. Hand grip strength was measured by using a hand grip dynamometer and expressed in kilograms. The strength was assessed by three times of the strong hand with patients seated upright with their elbow by their side and flexed at 90° so that their forearm was facing forward and resting on an armrest. In addition, laboratories, after overnight fasting included serum creatinine(Scr), alanine transaminase(ALT), aspartate transaminase(AST), gamma-glutamyl transpeptidase(GGT), cholesterol(CHO), low density lipoprotein-cholesterol(LDL-C), HDL-C, triglycerides(TG), fasting plasma glucose(FPG), fasting insulin(FINS), fasting C-peptide, HbA1c and urinalysis were collected on all study patients. Estimated glomerular filtration rate (eGFR) was derived from baseline serum creatinine level using the CKD Epidemiology Collaboration formula.<sup>10</sup>

### **2.3. Statistical Analysis**

Statistical analysis was conducted using SPSS 24.0 (SPSS Inc., Chicago, IL, USA). All data was checked for normality prior to analysis, presented as means (SD) for normally distributed variables and median (interquartile range) for variables without a normal distribution, respectively. ACR was categorized as normo- (ACR<30mg/g) and albuminuria (ACR≥30mg/g). Both anthropometry and biochemical measurements were compared between these two groups categorized by ACR levels, using analysis of variance (ANOVA) for normally distributed continuous data and non-parametric tests for variables without a normal distribution. Binary logistic regression analyses were carried out to evaluate the association of albuminuria and other clinical or biochemical variables. In addition, hand grip strength was categorized as low- (≤30kg) and high- (>30kg) hand grip strength groups and then Log(ACR), eGFR and Scr were compared between these two groups. The correlation between hand grip strength and log(ACR) was examined by Pearson's correlation analyses. P values<0.05 were considered statistically significant for all analyses.

### **3. Results**

#### **3.1 Characteristics of patients categorized according to ACR levels**

Characteristics of patients categorized according to ACR levels were showed in Table 1. Age(p=0.016), HbA1c(p=0.001), FPG(p=0.005), TG(p=0.045), Scr(p=0.001) and SBP(p<0.001) were all higher in correlation with higher levels of ACR, while hand grip strength(p=0.013) was the reverse. No significant differences were discovered among groups regarding FINS, fasting C-peptide, CHO, HDL-C, LDL-C, ALT, AST, body fat rate, BMI, DBP, HR and WHR.

#### **3.2 ACR and eGFR categorized according to the level of hand grip strength**

ACR and eGFR categorized according to the level of hand grip strength were demonstrated in Figure 1. Compared with that of patients with low-hand grip strength (≤30kg), Log(ACR) was significantly lower among patients with high-hand grip strength(>30kg)(p=0.025). However, no significant differences in eGFR were found between two groups(p=0.81).

#### **3.3 High hand grip strength was independently negatively correlated with the occurrence of abnormal albuminuria**

As Figure 2 demonstrated, using logistic regression analysis, it turned out that HbA1c (hazard ratio 1.42[1.18,1.70], P<0.001) as well as high systolic blood pressure (hazard ratio 2.41[1.34,4.32], P<0.001) were independent risk factors for the presence of albuminuria. Additionally, high hand grip strength (hazard ratio 0.37[0.17,0.81], P<0.001) was an independent protective factor for the presence of albuminuria, after adjusting for age, gender, HbA1c, weight, ALT, Scr, LDL and SBP.

#### **3.4 Correlation between hand grip strength and log(ACR)**

The relation of hand grip strength and ACR was compared by Pearson's correlation analyses. Figure 3 showed there was a negative correlation between hand grip strength and log(ACR).

#### **4. Discussion**

To our knowledge, this is the first cross-sectional study to examine the correlation between hand grip strength and albuminuria in Chinese patients with T2DM. The main finding of the current study is that hand grip strength was independently and negatively associated with albuminuria in Chinese type 2 diabetes patients, even after adjustment for further confounding factors.

The typical progressive course of diabetic nephropathy is initially developing an increase in albuminuria(microalbuminuria), progressing to macroalbuminuria, and, thereafter, a rapid decline in renal function.<sup>11</sup> The renal function was usually evaluated by eGFR. And transition in albuminuria class has been regarded as a hallmark of progression of diabetic kidney disease.<sup>12</sup> In our study, lower hand grip strength was strongly related to higher level of albuminuria, rather than estimated glomerular filtration rate(eGFR), which is consistent with a previous study. No significant differences were shown in low grip strength across the four eGFR categories.<sup>9</sup>Therefore, hand grip strength might be a useful method of identifying people who are at high risk of diabetic nephropathy in early stages. Besides, a previous prospective observational study of patients with all stages of CKD found that reduced grip strength was an independent predictor of death or progression to dialysis.<sup>13</sup>

Patients with high hand grip strength might have higher amounts of muscle mass. Since muscle is the primary site of glucose disposal, more muscle mass means less fluctuation of blood glucose level. Previous studies have suggested that greater HbA1c or glycemic variability could predict early stage of nephrology.<sup>14-15</sup> Improvement of glucose fluctuation may be involved in the protective effect of high hand grip strength on the presence of albuminuria.

Our findings could have meaningful public health implications, since hand grip strength is measured simply, fast, objectively and cheaply in clinical practice.

We acknowledged some limitations of this study. For one thing, the cross-sectional study design impeded the exploration of the cause-and-effect relationship between hand grip strength and ACR. For another, the existence of confounding factors and biases could hardly ruled out since the limited sample size and the specific race in this study. Therefore, further prospective cohort study with a larger sample size and various races, conducted in multicenter, as well as in non-diabetic population is required to confirm the association or even causal relationship.

#### **5. Conclusions**

This cross-sectional study provided evidence that high hand grip strength are associated with lower risk of the progression of albuminuria in Chinese patients with type 2 diabetes.

## **Declarations**

### **Ethics approval and consent to participate**

The study was approved by the Human Investigation Ethics Committee at Huashan Hospital, which conforms to the provision of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013). Written informed consent was obtained from all participants prior to commencing the study.

### **Availability of data and material**

The datasets of the current study is available from the corresponding author on reasonable request.

### **Competing interests**

All authors have no conflicts to declare.

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### **Authors' contributions**

Xiaoxia Liu designed experiments. Xiaoming Zhu performed data analysis. Yuanpin Zhang, Hangping Zheng, Wanwan Sun, Lijin Ji, Shuo Zhang, Qi Zhang, Yuetian Bai enrolled patients and performed the physical examination. Xiaoxia Liu, Yuanpin Zhang, Hangping Zheng wrote the initial manuscript draft.

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Table 1 Characteristics of patients categorized according to ACR levels

	ACR>30(N=15 0)	ACR<30(N=277)	P
Age(years)	71.37±8.07	69.46±7.36	0.016
Gender	1.45±0.49	1.50±0.50	0.034
Log(ACR)	2.0491±0.44	1.0590±0.26	<0.001
ACR	238.75±525.99	13.52±7.34	<0.001
HbA1C(%)	7.80±1.31	7.37±1.26	0.001
FINS(mU/L)	27.40±58.57	22.15±54.04	0.356
Fasting C-peptide( μ g/L)	0.86±0.42	0.83±0.61	0.595
FBG(mmol/L)	8.10±2.59	7.44±2.09	0.005
CHO(mmol/L)	4.67±1.12	4.88±3.27	0.435
TG(mmol/L)	1.99±1.45	1.75±0.95	0.045
HDL(mmol/L)	1.28±0.36	1.30±0.35	0.603
LDL(mmol/L)	2.51±0.89	2.61±0.94	0.306
eGFR(ml/min/1.73m <sup>2</sup> )	79.59±28.44	85.29±23.53	0.031
SCr( μ mol/L)	88.17±36.59	76.92±19.24	0.001
ALT(U/L)	22.36±17.68	23.07±15.85	0.672
AST(U/L)	20.22±12.26	20.32±9.84	0.926
GGT(U/L)	30.31±41.45	24.66±15.47	0.046
Body fat rate(%)	31.14±5.89	31.53±5.46	0.503
Hight(cm)	162.198.22	163.80±9.08	0.075
Weight(kg)	65.70±10.71	65.49±10.86	0.847

<b>BMI(Kg/m2)</b>	24.91±3.28	24.37±3.57	0.129
<b>SBP(mmHg)</b>	144.01±19.34	136.37±18.41	<0.001
<b>DBP(mmHg)</b>	78.66±12.27	80.14±45.71	0.705
<b>HR(bpm)</b>	77.39±11.03	75.92±10.99	0.218
<b>Waist circumference(cm)</b>	88.89±9.76	87.37±9.34	0.121
<b>Hip circumference(cm)</b>	96.07±8.61	95.75±8.48	0.716
<b>WHR</b>	0.92±0.06	0.91±0.05	0.077
<b>Neck circumference(cm)</b>	35.71±4.44	35.31±3.57	0.325
<b>Hand grip strength(kg)</b>	25.50±7.71	27.61±8.39	0.013

FBG: Fasting blood glucose, BMI: Body Mass Index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, WHR: Waist-to-hip Ratio

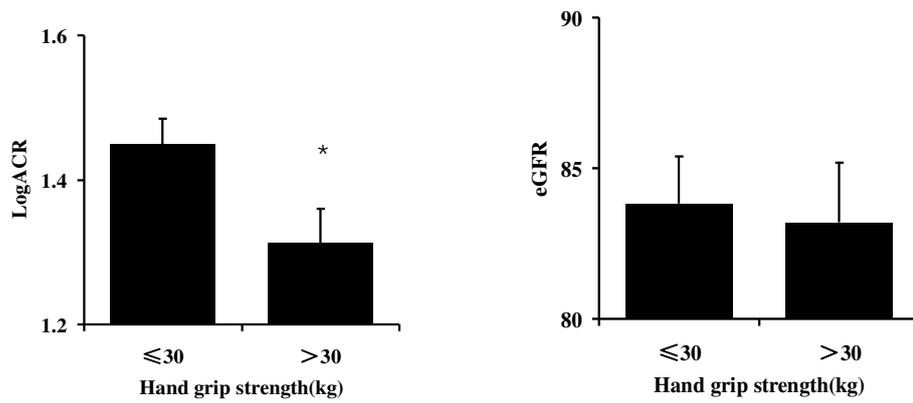


Fig 1: Log(ACR) was significantly lower with high-hand grip strength (>30kg) (\*p=0.025) compared with that of patients with low-hand grip strength (≤30kg). No significant differences in eGFR were found between two groups(p=0.81)

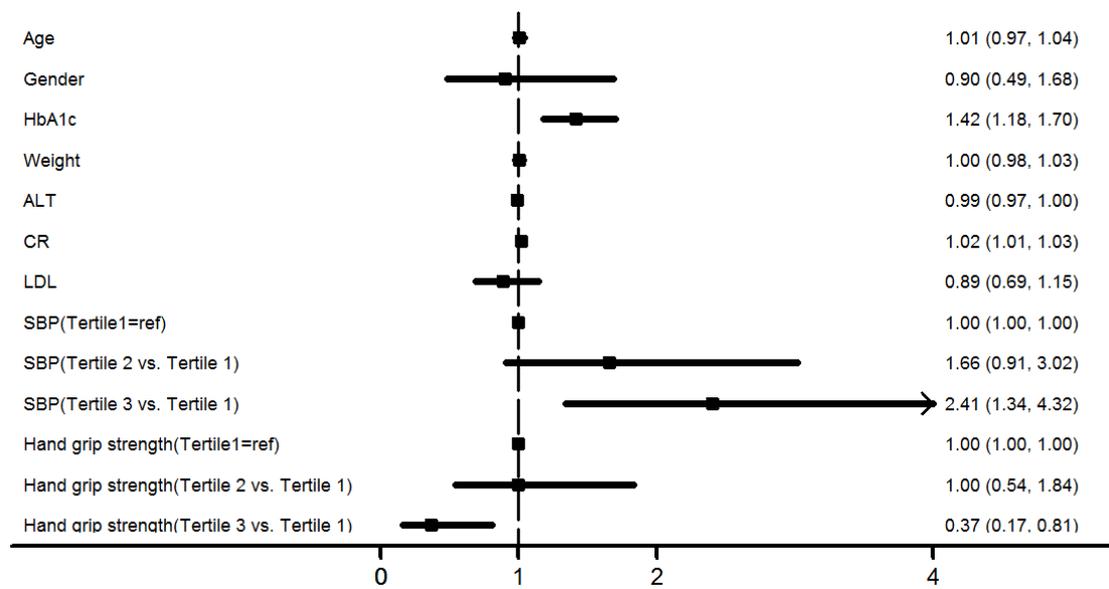


Fig 2. Logistic regression risk factor for albuminuria( $ACR \geq 30$ mg/g). HbA1c (hazard ratio 1.42[1.18,1.70],  $P < 0.001$ ) and high systolic blood pressure (hazard ratio 2.41[1.34,4.32],  $P < 0.001$ ) were independent risk factors for the albuminuria. High hand grip strength (hazard ratio 0.37[0.17,0.81],  $P < 0.001$ ) was an independent protective factor for the albuminuria, after adjusting for age, gender, HbA1c, weight, ALT, Scr (CR), LDL and SBP.

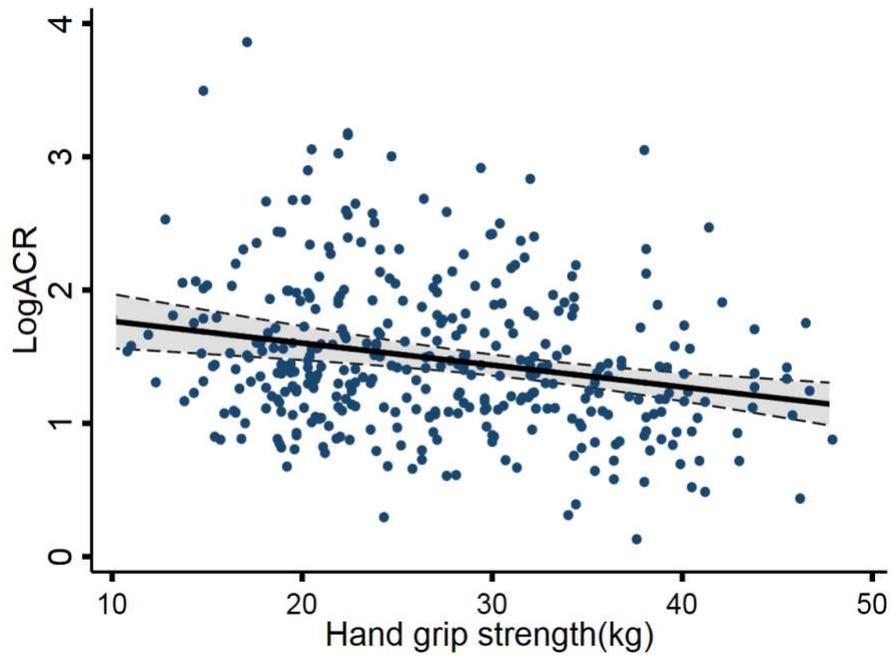


Fig 3. Hand grip strength and log(ACR) were negative correlated compared by Pearson's correlation analyses.