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Relationship between Inflammation and Handgrip Strength among Non-critical Inpatients

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Abstract **Purpose:** To analyze the relationship between inflammation and handgrip strength (HGS), an indicator of nutritional status, in inpatients with non-critical illnesses. **Materials and Methods:** HGS was measured in 530 inpatients (mean age = 56.4 ± 15.2 years) with a handgrip dynamometer. Nutrition risk was evaluated by administration of the nutrition risk screening–2002 tool. High-sensitivity C reactive protein (hs-CRP) measurements were made with an immuno-turbidimetric assay. Linear regression was used to assess relationships between variables. T-tests, Mann-Whitney U tests, and Kruskal-Wallis H tests were used to detect significant differences. **Results:** After accounting for gender, age, and nutrition risk, hs-CRP level was a significant predictor of HGS (β-coefficient = -0.1, $p < 0.05$). **Conclusion:** HGS was associated inversely with inflammation in hospitalized patients with non-critical illnesses. This finding suggests that relieving inflammation may benefit HGS, which could potentially lead to improved outcomes in terms of relief of inflammation, shorter hospital stays, decreased re-hospitalization rates, and decreased mortality rates.

Keywords: *HGS, inflammation, high-sensitivity-c reactive protein, inpatients, non-critical illness*

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1. Introduction

Handgrip strength (HGS) is a relevant indicator of patients' nutritional status. Numerous clinical and epidemiological studies have demonstrated the predictive value of HGS for short- and long-term mortality and morbidity, as well as for disease severity and outcome [1]. HGS has also been related to length of hospitalization and re-hospitalization rates. A study of 120 elderly patients (≥75 years old) suggested that HGS was inversely proportional to duration of hospital stay [2]. Furthermore, a 1-kg increase in HGS was associated with a 3% increase in likelihood of discharge to one's normal residence. Conversely, lower HGS at hospital admission was associated with a longer hospital stay and decreased probability of surviving to discharge [3].

In addition to gender, age, and nutrition, HGS was found to be closely related to inflammatory activity in inpatients [4]. Inflammation has been suggested to affect skeletal muscle metabolism and reduce HGS [5,6,7]. In this study, we investigated whether levels of the inflammatory marker C reactive protein (CRP) [8], as determined by a high-sensitivity C reactive protein (hs-CRP) test, are associated with HGS among inpatients.

2. Materials and Methods

2.1. Cases

A total of 530 inpatients (299 males and 231 females) that were treated at the medical wards in Beijing Friendship Hospital from June 1st to December 31st, 2012 were enrolled consecutively. Patient ages ranged from 18 years to 87 years; the mean age was 56.4 ± 15.2 years. Patients were recruited from the following departments: respiratory medicine (19.6%, n = 104), cardiology (14.5%, n = 77), neurology (15.7%, n = 83), hematology (4.5%, n = 24), nephrology (4.9%, n = 26), gastroenterology (5.1%, n = 27), hepatic medicine (19.6%, n = 104), endocrinology (4.7%, n = 25), other departments (11.3%, n = 60). The experimental protocol was established in accordance with the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Beijing Friendship Hospital. Written informed consent was obtained from each participant.

2.2. Inclusion and Exclusion Criteria

Patients were required to meet the following inclusion criteria: 1) 18–90 years of age, 2) able to stand and perform vertical HGS measurements independently, 3) presented with a non-critical illness (critical illnesses require immediate or intensive treatments). Patients were excluded from the study if they were pregnant, had hemiplegia, neuromuscular diseases, coma, osteoarthropathy, moderate-to-severe neurological cognitive impairment or retinal detachment.

2.3. HGS Measurements

HGS was measured by a mechanical handgrip dynamometer (Xiangshan dynamometer EH101, Zhongshan,

Guangdong, China) within 24 hours after admission. After explaining the procedure to each patient, HGS measurements were performed and recorded. Patients were standing upright. They held the dynamometer with their palms inward and the dynamometer display outward. The dynamometer did not touch patients' trunk or clothing during measurements. Patients were encouraged to perform a maximal isometric contraction. The maximum HGS value with the dominant hand was recorded [9].

2.4.Nutrition Risk Screening

Age, body mass index (BMI), nutrition intake, amount of recent weight loss, changes in diet, and diagnosis were determined within 24 hours after admission by patient surveys. BMI was calculated from height and weight data obtained from anthropometric measurements. Nutrition risk was scored according to the Nutritional Risk Screening 2002 guidelines (NRS 2002). Patients with final scores ≥3 were considered to be at nutritional risk [10].

2.5. Anthropometric Measurements

Patients were weighed to the nearest 0.1 kg using an electronic scale (Suhong RGZ-120, Jiangsu, China) while wearing light clothing. Height was measured with a stadiometer (Suhong RGZ-120, Jiangsu, China) to the nearest 0.1 cm. BMI was expressed as the ratio of weight (in kg) over the square of height (in m). A BMI < 18.5 kg/m^2 was considered to be underweight [11].

2.6. hs-CRP Assay

Concentrations of hs-CRP were determined within 24 hours after admission by an automated biochemical analyzer (Hitachi 7600, Japan). The normal range for hs-CRP results was considered to be 0–3 mg/L.

2.7. Quality Control

The study was designed and conducted by doctors and dietitians at the Beijing Friendship Hospital to ensure that the investigation was feasible and results would be valid. Training and pilot experiments were performed prior to data acquisition.

2.8. Statistical Analysis

Linear regression was used to assess the relationships between variables. T-tests, Mann-Whitney U tests, and Kruskal-Wallis H tests were used to test for significant differences. All statistical analyses were performed with the Statistical Package for Social Sciences for Windows (SPSS, version 16.0; SPSS, Inc., an IBM Company, Chicago, IL). Results were considered significant when p values were <0.05.

3. Results

3.1. General Conditions

The baseline characteristics of the study are summarized in Table 1. The total number of patients was 530 (299 men, 56.4%; 231 women, 43.6%). The mean hs-CRP level was 6.8 ± 18.2mg/L, and hs-CRP levels ranged from 0 to 160 mg/L. Most patients (358; 67.5%) had normal hs-CRP values (0–3 mg/L), which represents normal amounts of inflammation. A total of 172 patients (32.5%) had values above 3 mg/L that indicated high levels of inflammation.

Table 1. Characteristics of the study sample

Parameter	All (N = 530)	Males (N = 299)	Females (N = 231)	*p*-value
Age (y)	56.4 ± 15.2	58.3 ± 14.6	53.9 ± 15.6	0.001
BMI (kg/m^2)	26.5 ± 18.1	26.5 ± 17.1	26.5 ± 19.5	0.985
HGS (kgF)	29.2 ± 10.1	34.2 ± 9.3	22.7 ± 6.8	<0.001
hs-CRP (mg/L)	6.8 ± 18.2	4.1 ± 14.6	10.3 ± 21.5	<0.001
Nutrition screening score (n)	0.6 ± 0.8	0.6 ± 0.9	0.4 ± 0.7	0.003

Abbreviations: BMI, body mass index; HGS, hand grip strength; hs-CRP, high-sensitivity-C reactive protein.

The mean HGS was 29.2 ± 10.1 kgF and ranged from 6.5 kgF to 60.4 kgF. Values of HGS, hs-CRP, and nutrition risk score were significantly different between male and female patients (p < 0.05). Female patients had lower HGS, lower nutrition risk screening scores, and higher hs-CRP values than male patients (Table 1). Values of HGS values differed relative to age strata (18–45, 45–60, 60+) in both male (χ^2=45.258, p < 0.001) and female (χ^2=22.339, p < 0.001) patients. Both male and female patients in the 45–60-year-old age band showed the highest HGS, while those in the ≥60-year-old age band had the lowest HGS (Table 2).

Table 2. HGS of study sample according to sex and age strata.

Sex	HGS (kgF)			*p*-value
	18-45 y	45-60 y	60-y	
Males	37.3 ± 9.9	38.6 ± 11.5	30.6 ± 7.9	<0.001
Females	23.9 ± 5.1	25.5 ± 7.4	20.2 ± 6.5	<0.001

¶Abbreviations: HGS, hand grip strength.

3.2. Relationship between Inflammation Levels and HGS of Patients

The HGS of patients with no or mild inflammation (hs-CRP 0–3 mg/L) differed significantly from the HGS of patients with clinically concerning inflammation (hs-CRP > 3 mg/L) (31.9 ± 0.5 *vs*. 23.4 ± 0.8 kgF, U = 14610, W = 29488, p < 0.001). HGS was inversely related to inflammation levels. Bivariate correlational analysis showed a strong association between hs-CRP level and HGS (r = -0.552, p < 0.001). Furthermore, linear regression analysis also revealed a significant linear relationship between hs-CRP level and HGS (β-coefficient = -0.2, p < 0.001). As shown in Table 3, we observed an independent inverse association between hs-CRP level and HGS (p < 0.05). The following variables also emerged as risk factors or potential confounders: age, sex, and nutrition risk screening score (p < 0.05).

Table 3. Analysis of factors influencing HGS

Factor	HGS (kgF)	
	β-coefficient	*p*-value
Age strata (y)	-2.0	<0.001
Sex	-11.3	<0.001
Nutrition screening score (n)	-2.5	<0.001
hs-CRP (mg/L)	-0.1	<0.001

¶Abbreviation: hs-CRP, high-sensitivity C reactive protein; HGS, hand grip strength.

4. Discussion

The linear regression results presented here show significant impacts of age, sex, nutritional status, and inflammation on HGS, consistent with previous studies [12,13,14,15,16]. Several studies have shown that people experience a gradual loss of muscle mass and strength after the age of 40 at a rate of 1.5–3.5% per year [9]. Undernourished patients (identified by NRS-2002) also had lower than typical HGS [14]. Results from animal experiments have suggested that inflammation induces muscle weakness [15,16].

There are two possible clinical mechanisms responsible for the association between inflammation and HGS. First, inflammation increases production of cytokines, such as CRP, interleukin-6,and tumor necrosis factor-α, which can lower HGS by reducing muscle protein synthesis, increasing skeletal muscle breakdown, altering the resting membrane potential of skeletal muscle, and decreasing contractility [15,16]. Second, inflammation and diseases may affect appetite, which can reduce the intake of protein and affect the conversion of ATP to creatine phosphate, thereby reducing the available energy supply (see Figure 1). Results from other studies [17,18] have also suggested that malnutrition was prevalent among inpatients. In addition to disease, over- or undernutrition can also cause inflammation. Moreover, HGS, which reflects nutritional status, has been found to correlate with length of hospital stay, mortality and re-hospitalization rates, and outcomes [1]. Hence, making reasonable nutritional support a clinical priority may help reduce inflammatory activity and, ultimately, affect muscle metabolism, enhance muscle strength, and improve quality of life of patients, especially those who are at nutritional risk.

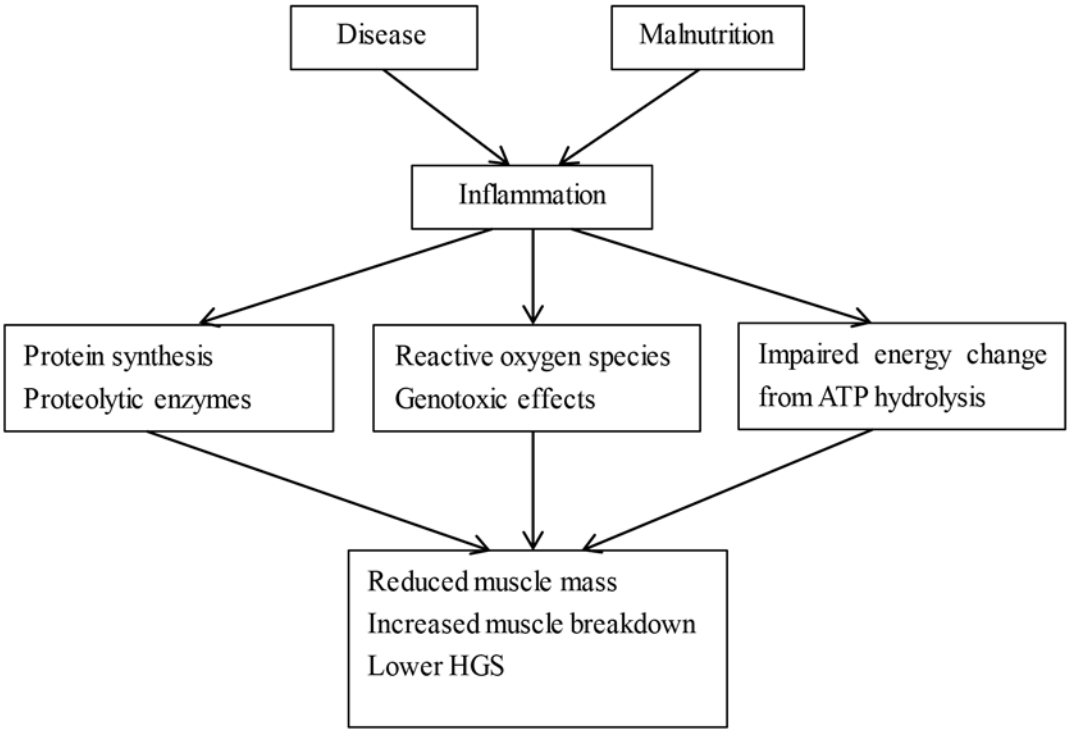

Figure 1. Hypothesis of the pathogenesis of impaired muscle function during inflammation

The association between inflammation and muscle strength has been well-studied in patients with critical illnesses for whom inflammation decreases muscle strength. However, this relationship in the non-critically ill has not been thoroughly investigated. This study showed a significant association between HGS and hs-CRP test results in patients with non-critical illnesses after excluding the effects of confounders (i.e. age, sex, BMI, and nutrition risk screening scores).

We did not analyze the quantitative impact of each hs-CRP level (0–3 mg/L and > 3 mg/L) on HGS. Also, several factors that may affect HGS were not addressed in this study, such as fat-free mass, manual labor intensity, and disease. In the future, more detailed studies should be conducted to examine the relationship between inflammation and HGS.

In conclusion, we observed a significant association between inflammation and HGS in hospitalized patients with non-critical illnesses. Relieving inflammation may help to improve HGS and recovery of HGS may lead to improved outcomes with respect to relieving inflammation, shorter hospital stays, decreased re-hospitalization rates, and decreased mortality rates [1,2,3]. In future studies, we will investigate in depth whether and how nutrition

support can improve patients' nutritional status and relieve inflammation and the association of such support with HGS and disease recovery.

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Conflicts of Interest

The authors have no financial conflicts of interest.

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