Title:

Associations between Grip Strength and Glycemic Control in Type 2 Diabetes Mellitus: the 2014–2019 Korea National Health and Nutrition Examination Survey

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Conflict of Interest:

The authors have no conflicts of interest to declare for this study.

Author Contributions:

Conceptualization: HC, YSK. Data curation: HC, HS, GHK. Formal analysis: HC, HS, GHK. Funding acquisition: YSK. Methodology: HC, HS, GHK, YSK. Visualization: HC, HS, GHK. Writing–original draft: HC, HS, GHK. Writing–review & editing: HS, GHK, OL, HYM, YSK.

Abstract

Objectives:

Glycemic control is essential to prevent severe complications in patients with diabetes mellitus. This study aimed to determine the association between grip strength and glycemic control in Korean adults with type 2 diabetes mellitus.

Method:

From the Korea National Health and Nutrition Examination Survey, 2,498 participants aged over 19 years without a history of cardiovascular disease and cancer were selected for analysis. Grip strength was assessed using a handheld dynamometer and was represented as age- and sex-specific tertiles. Multivariable logistic regression was performed to calculate the odds ratio and 95% confidence interval of glycemic control according to the grip strength tertiles.

Results:

Our results showed that the lowest group of grip strength had a significant OR of 0.67 (95% CI, 0.47–0.97), compared to the highest tertile of grip strength. Furthermore, the significant associations between grip strength and glycemic control were presented only in men and not in women.

Conclusions:

In conclusion, lower grip strength was associated with poor glycemic control in patients with diabetes mellitus, especially in men. However, further studies are needed to confirm the causal relationship between grip strength and glycemic control.

Keywords: hand strength, muscle strength, glycated hemoglobin A

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic condition that maintains high blood glucose levels and is a cause of complications, such as cardiovascular disease (CVD), kidney failure, retinopathy, and peripheral diseases [1]. The International Diabetes Federation projected that the prevalence of T2DM will be 51% higher in 2045 compared to 2019 [1]. Also, T2DM is a major public health problem in Korea, with its prevalence increasing every year from 2005 to 2015 [2]. In addition, T2DM was the ninth cause of global death in 2019, and it was the sixth leading cause of death in Korea [3, 4].

Hemoglobin A1c (HbA1c) was used to confirm whether blood glucose was regularly controlled in diabetic

patients [5, 6]. T2DM patients with higher HbA1c levels had increased risk of developing CVD and mortality compared to diabetic patients with lower HbA1c level [7, 8]. Therefore, diabetic patients are continuously recommended to control their blood glucose levels to prevent complications [9]. However, 65.0% of Korean adults with diabetes were aware that they had been diagnosed with diabetes, but only 28.3% of diabetic patients were able to achieve glycemic control [10].

The skeletal muscles are the primary storage site of plasma glucose, which is converted to glycogen, and are the most prominent protein reservoir [11]. In this regard, insulin metabolizes both plasma glucose and protein in skeletal muscle [11, 12]. Moreover, muscular strength, a characteristic of skeletal muscles, is an essential component of physical fitness [13] and can only be improved by long-term exercise [14]. Unfortunately, muscular strength decreases with age [15]. As demonstrated in previous studies, muscular strength is inversely associated with the risk of mortality [16], CVD [17], and cancer [18]. Furthermore, diabetic patients with lower muscular strength had a significantly higher risk of mortality and CVD incidence than those with higher muscle strength [19]. Also, low muscular strength was associated with deleterious indices, representing the higher risk of atherosclerosis and diabetic peripheral neuropathy in patients with diabetes [20, 21].

To date, there have been few studies on the association between grip strength and glycemic control in T2DM. Moreover, it has not been examined in Korean adults. Therefore, this study aimed to determine the association between grip strength and glycemic control in patients with diabetes mellitus.

2. Materials and Methods

Study participants

This study analyzed data from the Korea National Health and Nutrition Examination Survey (KNHANES) 2014–2019. The KNHANES is conducted annually by the Korea Center for Disease Control and Prevention to collect information about the health behavior, prevalence of chronic diseases, and nutritional status of the Korean population [22]. Specifically, from 2014 to 2019, KNHANES surveyed a total of 45,022 participants. Individuals with T2DM, aged 19 years or older, and non-pregnant women were included in the current study (n=4,173). Moreover, participants were excluded if they reported a history of CVD or cancer (n=643) and did not undergo HbA1c or grip strength measurement (n=348). Furthermore, those who had missing data for the covariates (n=684) were excluded. Finally, 2,498 participants were selected for this study (Fig 1).

Grip strength

Grip strength was assessed in a standing position without bending the elbow or wrist, and the handle was

adjusted to 90 degrees with the second finger joint. Three measurements were performed for both hands using a digital handheld dynamometer (T.K.K.5401; Takei Scientific Instruments Co, Ltd, Tokyo, Japan), with 1-min intervals between trials [23]. Grip strength (kg/BMI) was calculated as the mean of the maximum values of both hands [19, 24], and was divided by the body mass index (BMI) [25]. In addition, grip strength was categorized into age- and sex-specific tertiles (upper, middle, and lower) for considering the biological differences within the sex and age groups (Supplementary Material 1).

T2DM and glycemic control

T2DM was defined as fasting plasma glucose levels ≥ 126 mg/dL among individuals who maintained fasting status over 8 h or HbA1c $\geq 6.5\%$ [26]. HbA1c is generally used to diagnose T2DM because it indicates the glycemic status in the last 2–3 months. As such, it was used to confirm the typical blood glucose level in diabetic patients [5]. Thus, this study defined glycemic control in individuals diagnosed with T2DM but had HbA1c $< 6.5\%$ [27, 28].

Covariates

The following confounding factors were adjusted: age, sex, educational status (elementary school, middle school, high school, $\geq$ undergraduate), household income (low, middle-low, middle-high, high), smoking status (current, former, never), alcohol intake ($\geq$ once per month in the recent year, $<$ once per month in the recent year, never), family history of T2DM (yes, no), obesity ($18.5 \leq$ normal < 23 , $23 \leq$ overweight < 25 , $25 \leq$ obese) [29], hypertension, hypercholesterolemia, and insulin use (yes, no). The household income was categorized into age- and sex-specific quartiles based on equalized household income by the following calculation that monthly household income divided by the square root of the numbers of household members. In addition, the criteria for diagnosing hypertension and hypercholesterolemia were as follows: systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg and total cholesterol ≥ 240 mg/dL or use of anti-hypercholesterolemic drugs, respectively. In addition, the use of insulin for glycemic control was reported by the participants in the questionnaire [30].

Statistical analysis

According to grip strength levels, continuous variables are presented as mean and standard error (SE), while categorical variables are presented as frequencies and proportions (weighted %) to describe subjects' characteristics. The one-way analysis of variance and chi-square tests were used to analyze the differences between the groups. Multivariate logistic regression was used to examine associations between grip strength and glycemic control in diabetic patients, and the results are reported as the odds ratio (OR) and 95% confidence

interval (95% CI). Multivariate logistic regression analysis was adjusted for age and sex in Model 1, for the potential confounders in Model 2, and for the use of insulin in Model 3. All analyses were performed using the upper grip strength group as a reference group. Statistical significance was set at $p < .05$. Statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute, Cary, North Carolina).

Ethics statement

This study was approved by the Institutional Review Board of Seoul National University (No. E2105/002-007).

3. Results

Table 1 shows the characteristics of the participants based on the tertiles of grip strength. The proportion of participants with a low education status, low household income, obesity, hypertension, and insulin use were higher in the lowest level of grip strength, while those who finished undergraduate studies and have a family history of T2DM were more frequent in the middle level of grip strength. The proportion of patients with a high level of household income and alcohol intake of more than once was high in the upper level of grip strength.

Table 2 shows the results of the multivariate logistic regression analysis of associations between grip strength and glycemic control in diabetic patients. The lowest and middle levels of grip strength had significant ORs of 0.65 (95% CI, 0.45–0.93) and 0.72 (95% CI, 0.52–0.99), respectively, compared to the highest level of grip strength after adjustment for confounders. Additionally, after adjusting for insulin use, the OR for the lowest level of grip strength was 0.67 (95% CI, 0.47–0.97). Nevertheless, the linear trend across the tertiles of grip strength was statistically significant (p for trend = 0.031), though the middle level of grip strength had a statistically insignificant association (OR, 0.73; 95% CI, 0.53–1.01). In the analyses that considered the continuous variables (increment per 0.05 kg/BMI), a significant association was observed after adjusting for the confounders (OR, 1.03; 95% CI, 1.01–1.06).

Figure 2 shows the results of the subgroup analyses based on sex. In men, lower and middle levels of grip strength had statistically significant ORs of 0.60 (95% CI, 0.38–0.95) and 0.64 (0.42–0.97), respectively, after adjusting for the confounders. However, the significant association between grip strength and glycemic control was not observed in women.

4. Discussion

This was the first study to analyze the association between grip strength and glycemic control in Korean adults

with T2DM, including a large population aged 19-80 years. The multivariate logistic regression analyses showed that the lowest level of grip strength had a significantly lower probability of glycemic control after adjusting for all confounding variables, including insulin use.

These findings were inconsistent with those of a previous study [30, 31]. The previous study analyzed the data of 1,058 participants aged over 40 years and reported that grip strength was associated with glycemic control after adjusting for covariates, such as biological, behavioral, dietary, educational, and socioeconomic variables ($p = 0.073$ for linear trend). However, after adjusting for additional insulin use, no significant association was observed [30]. Similarly, a study with 768 T2DM patients found that a higher HbA1c level ($\geq 8.0\%$) was not associated with weak grip strength after adjustment for confounders [31]. These differences may be due to the following reasons: the previous studies were performed using data from Americans or Japanese patients aged over 40 years; for the dependent variable, they used HbA1c above 7% as the criterion of poor glycemic control and a dichotomous criterion for weak grip strength (<26 kg for men and <18 kg for women); relative grip strength was used in this study, but the previous studies used absolute grip strength for their analyses. However, other observational studies on diabetic patients over 40 years have shown that poor glycemic control was associated with lower muscle quality and mass [31-33].

Furthermore, subgroup analyses across sexes were performed in this study. The results showed that both the middle and upper levels of grip strength were associated with glycemic control only in men and not in women. These sex differences in our results may be explained by the differences in body composition. Generally, healthy women had more risk factors facilitating insulin resistance, including less muscle mass and a higher level of lipids in the muscle cells than men [34, 35]. In addition, compared to men, women have a lower percentage of muscle mass in the upper extremities [36, 37]. Thus, grip strength may be a more suitable indicator for men.

Insulin resistance is the primary metabolic defect in T2DM patients, and most diabetic patients have severe insulin resistance in skeletal muscles [11, 38]. In addition, insulin resistance is negatively correlated with muscular strength, which has been well established in previous studies [39, 40]. Generally, by inhibiting the binding of insulin with its receptor, insulin resistance impairs glycogen synthesis by suppressing insulin's stimulation of the glucose transport system in the muscles and inhibits the protein synthesis pathway, which is responsible for muscle hypertrophy [41, 42]. Therefore, severe insulin resistance causes impaired glucose metabolism and muscle atrophy in patients with T2DM [41, 42], leading to a decline in muscular strength [43]. Consequently, low muscular strength and insulin resistance likely have deleterious effects on each other.

Plasma glucose enters the muscle cell by GLUT 4 either through the IRS/PI3K/Akt pathway or through muscle

contraction (*i.e.*, insulin-dependent and insulin-independent pathways) [44, 45]. As mentioned above, most diabetic patients' insulin-dependent pathway is affected by insulin resistance, but the insulin-independent pathway is not damaged and appears to maintain a normal function [46]. An experimental study consistently showed that the GLUT 4 level increased by 40% in the leg trained with resistance exercise compared to the untrained leg [47]. Thus, increased GLUT 4 levels can promote glucose disposal in the trained skeletal muscle [44]. Although there is a lack of evidence, differentiation in the severity of insulin resistance and GLUT 4 content in the skeletal muscle likely contributes to glucose metabolism in T2DM.

Our study had the following limitations. First, because the KNHANES only includes data from the Korean population, these results may not be generalizable to other countries. Second, since this was a cross-sectional study, we could not determine the causal relationship between grip strength and glycemic control in patients with T2DM. Lastly, the duration of diabetes affecting glycemic control was not adjusted in the current study. As for the strengths of this study, it was the first examination of the association between grip strength and glycemic control in approximately 2,500 diabetic patients after excluding individuals diagnosed with the disease using data representative of Korean adults. However, further studies are needed to investigate the causal relationship between grip strength and glycemic control in diabetes in future cohort studies involving Korean adults.

5. Conclusion

Grip strength is a valuable indicator in the clinical field due to its simplicity and inexpensiveness compared to the other methods that measures muscular strength. Our results showed that the lowest and middle levels of grip strength were significantly associated with a 40% and 36% lower probability of glycemic control in men with diabetes, respectively. Thus, our findings suggest that lower grip strength could be a valuable indicator for identifying those with the highest risk of poor glycemic control in diabetic patients, especially in men. However, further longitudinal studies are needed to elucidate the causal relationship and the reasons for the sex difference.

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1 Table 1. Characteristics of participants in KNHANES, 2014-2019 according to grip strength tertiles

Characteristics	Grip Strength			<i>p</i> -value
	Upper (n=834)	Middle (n=836)	Lower (n=828)	
Weighted N	854,815	850,579	824,702	
Age	56.71±0.52	56.87±0.55	57.64±0.58	0.463
Sex				0.965
Men	436 (58.1)	438 (57.9)	433 (57.4)	
Women	398 (41.9)	398 (42.1)	395 (42.6)	
Education				0.003
Elementary school	227 (21.5)	262 (24.1)	291 (29.1)	
Middle school	131 (15.8)	131 (15.2)	138 (14.9)	
High school	301 (40.1)	262 (34.7)	220 (29.3)	
Undergraduate	175 (22.5)	181 (26.0)	179 (26.6)	
House income				<.001
Low	183 (17.3)	219 (23.3)	260 (27.3)	
Middle low	233 (26.8)	242 (29.3)	227 (27.7)	
Middle high	210 (28.7)	186 (23.0)	182 (23.8)	
High	208 (27.2)	189 (24.5)	159 (21.2)	
Obesity				<.001
Normal	326 (38.3)	160 (18.8)	85 (9.3)	
Overweight	235 (27.5)	222 (25.7)	134 (14.5)	
Obese	273 (34.2)	454 (55.5)	609 (76.2)	
Smoking				0.392
Never	429 (46.1)	442 (49.5)	434 (49.0)	
Former	236 (29.5)	220 (26.8)	208 (24.7)	
Current	169 (24.4)	174 (23.7)	186 (26.3)	
Alcohol				0.012
Never	111 (11.4)	131 (12.9)	161 (16.8)	
< once per month	272 (30.7)	263 (29.7)	288 (32.6)	
≥ once per month	451 (58.0)	442 (57.4)	379 (50.6)	
Family history				0.465
Yes	234 (31.7)	258 (35.0)	233 (32.7)	
No	600 (68.3)	578 (65.0)	595 (67.3)	
Hypertension				<.001
Yes	409 (45.3)	500 (55.9)	545 (62.2)	
No	425 (54.7)	336 (44.1)	283 (37.8)	
Hypercholesterolemia				0.246
Yes	342 (38.2)	324 (36.9)	335 (41.3)	
No	492 (61.8)	512 (63.1)	493 (58.7)	
Insulin use				0.007
Yes	33 (3.1)	38 (4.1)	59 (6.5)	
No	802 (96.9)	798 (95.9)	769 (93.5)	

2 Values are presented as Mean±SE or No. (weighted %).

3

4 Table 2. Associations between grip strength and glycemic control

Grip Strength	N	cases	Odds Ratio (95% Confidence Interval)		
			Model 1	Model 2	Model 3
Upper	834	147	1 (reference)	1 (reference)	1 (reference)
Middle	836	118	0.75 (0.55-1.02)	0.72 (0.52-0.99)	0.73 (0.53-1.01)
Lower	828	106	0.69 (0.50-0.95)	0.65 (0.45-0.93)	0.67 (0.47-0.97)
<i>p</i> for trend			0.021	0.018	0.031
Increment per 0.05 kg/BMI			1.03 (1.01-1.06)	1.04 (1.01-1.07)	1.03 (1.01-1.06)

5 Values are presented as ORs (95% CI).

6 Model 1 was adjusted for age, sex.

7 Model 2 was adjusted for model 1 plus education, house income, current smoking, alcohol, family history, obesity,
8 hypertension, and hypercholesterolemia.

9 Model 3 was adjusted for model 2 plus insulin use.