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Relative Handgrip Strength Positively Correlates with Low-Density Lipoprotein Cholesterol Level in Patients with Type 2 Diabetes: A Cross-Sectional Study

ABSTRACT

Objective: The aim of this clinical study was to discover a new factor affecting muscle strength and quality in patients with type 2 diabetes (T2D).

Materials and methods: The relationship between muscle strength and quality and low-density lipoprotein cholesterol (LDL-C), random triglyceride (TG), and high-density lipoprotein cholesterol (HGL-C) levels were studied. Relative handgrip strength (RHGS) was used to evaluate muscular strength and quality. RHGS was calculated by dividing the absolute handgrip strength by body mass index (BMI). Using the stepwise method, multiple regression analysis was conducted and the linear correlation between variables was calculated by estimating Pearson correlation coefficient.

Results: This study enrolled 68 patients with T2D. The majority of the participants were men, accounting for 71.5%. The median values of the measured parameters were as follows: age 67 years, physical activity level 10.1 METs/h/week, estimated glomerular filtration rate 57.0 mL/min/1.73 m^2, systolic blood pressure 123.5 mmHg, diastolic blood pressure 69.0 mmHg, body weight 64.1 kg, body mass index 24.35 kg/m^2, HbA1c level 7.4%, random TG level 139 mg/dL, HDL-C level 52.5 mg/dL, and T2D duration 16.0 years. RHGS was 1.47 ± 0.40 kg/BMI. RHGS was associated with LDL-C (r = 0.349) but was not correlated with random TG and HDL-C (r = 0.124 and r = 0.088, respectively).

Conclusions: Patients with T2D with better muscle strength and quality demonstrated an increased LDL-C level. In patients with T2D, LDL-C may be a factor affecting muscle strength and quality. (Clin Diabetol 2024; 13, 3: 180–184)

Keywords: relative handgrip strength, low-density lipoprotein cholesterol, type 2 diabetes

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Introduction

Type 2 diabetes (T2D) is a progressive disease characterized by insulin resistance and continuous loss of endogenous insulin secretion [1]. Furthermore, T2D is associated with sarcopenia, which results in the loss of whole-body homeostasis and decline in physical function [2]. Sarcopenia-derived muscle weakness is consistently associated with deterioration of glucose metabolism in patients with diabetes, even among well-nourished subjects [3, 4]. Relative handgrip strength (RHGS) has been proposed as a diagnostic tool for assessing muscular strength and quality, including in overweight individuals [5]. In this clinical study, the relationship between muscle strength and quality and low-density lipoprotein cholesterol (LDL-C), random triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels was studied in patients with T2D to search for a new factor affecting RHGS in patients with T2D as the relationship between RHGS and LDL-C in patients with T2D is inconclusive.

Materials and methods

Participants

Our study protocol was reviewed and approved by the Institutional Review Board of Hoshi-iin as 3–1 (March 31, 2021). Written informed consent was obtained from each participant.

We excluded participants who had been diagnosed with type 1 diabetes (n = 1). Also, patients with orthopedic diseases such as chronic rheumatoid arthritis or cerebrovascular diseases with paralysis were excluded (n = 1 and n = 2, respectively).

Patients consistently visited the hospital for follow-up examinations once a month. Using the same random blood samples as previously reported, the patients' lipid profiles, plasma glucose levels, and glycated hemoglobin (HbA1c) levels were measured [6]. When patients visited the hospital, a registered nurse and registered dietician advised on the necessary dietary and lifestyle modifications.

Definition of T2D

Diabetes is defined as a fasting plasma glucose of 126 mg/dL or greater and/or a 2-h glucose level of 200 mg/dL or greater during a 75-g OGTT [7]. Anti-glutamic acid decarboxylase antibody was negative and insulin secretion was not depleted in all participants.

Handgrip strength and RHGS measurement

Using a digital grip strength dynamometer (Model T.K.K 5401; Takei Scientific Instruments Co., Tokyo, Japan, measurement range: 5.0–100.0 kg), handgrip strength was measured in each hand three times [8]. The participants were instructed to hold the dynamometer with the second proximal interphalangeal joint of the hand flexed at 90° to the handle and squeeze the handle as hard as they could in the standing position (elbow extension status). The participants rested for at least 30 s after each measurement. The maximum value of the three measurements was used [9].

RHGS was used for assessing muscular strength and quality. RHGS was calculated by dividing the absolute handgrip strength by body mass index (BMI) [10].

Statistical analysis

All statistical data were analyzed using the SPSS software (version 10.0, SPSS Inc., Chicago, IL, USA). All numerical values are expressed as mean ± standard deviation. Using the stepwise method, multiple regression analysis was conducted with a software program. We calculated Pearson correlation coefficient to estimate the linear correlation between variables.

Results

Participant characteristics

This study enrolled 68 patients with T2D who visited our hospital in April 2022. Patient characteristics are shown in Table 1. The majority of the participants were men, accounting for 71.5%. The median values of the measured parameters were as follows: age 67 (range 24–94) years, body weight 64.1 (range 45.7–136.2) kg, BMI 24.35 (range 17.9– 42.2) kg/m^2, HbA1c level 7.4% (range 5.8–12.8), random TG level 139 (range 53–493) mg/dL, HDL-C level 52.5 (range 36–119) mg/dL, LDL-C level 104.8 (range 30–174) mg/dL.

Proportion of patients prescribed with antidiabetic, antihypertensive, and antihyperlipidemic medications

The proportion of patients prescribed antidiabetic medications are shown in Table 2. The proportion of prescribed antidiabetic medications was as follows: sodium-glucose cotransporter 2 inhibitors, biguanides, insulin, sulfonylureas, dipeptidyl peptidase-4 inhibitors, α- glucosidase inhibitors, GLP-1 receptor analogs, and glinides were prescribed in 40.5%, 43.2%, 54.1%, 2.7%, 37.8%, 29.7%, 27.0%, and 48.6% of patients, respectively, while no thiazolidinedione was prescribed.

Antihypertensive and antihyperlipidemic drugs were prescribed in 72.2% and 61.1% of patients, respectively.

Analysis of multiple comparisons for factors affecting RHGS

RHGS was 1.47 ± 0.40 kg/BMI. Stepwise multiple regression analysis demonstrated that the LDL-C was

Table 1. Characteristics of the Study Participants

	Median value	Range
Age [years]	67	24–94
Physical activity level [METs/h/week]	10.1	3.0–20.8
Estimated glomerular filtration rate [mL/min/1.73 m^2]	57.0	33.0–93.0
Systolic blood pressure [mmHg]	123.5	93–191
Diastolic blood pressure [mmHg]	69.0	47–101
Body weight [kg]	64.1	45.7–136.2
Body mass index [kg/m^2]	24.35	17.9– 42.2
Glycated hemoglobin (HbA1c) [%]	7.4	5.8–12.8
Random triglyceride (TG) [mg/dL]	139	53–493
High density lipoprotein cholesterol (HDL-C) [mg/dL]	52.5	36–119
Low density lipoprotein cholesterol (LDL-C) [mg/dL]	104.8	30–174
Duration of type 2 diabetes (T2D) [years]	16.0	4–45

Table 2. Proportion of Patients Prescribed Antidiabetic Medications

Sodium glucose cotransporter inhibitors (%)	40.5
Biguanides (%)	43.2
Insulin (%)	54.1
Sulfonylureas (%)	2.7
Dipeptidyl peptidase-4 inhibitors (%)	37.8
α-glucosidase inhibitors (%)	29.7
Glucagon-like peptide 1 analogs (%)	27.0
Glinides (%)	48.6
Thiazolidinedione (%)	0

a significant determinant of RHGS and not TG and HDL-C ($r = 0.349$, $p < 0.001$, $r = 0.130$, $p =$ not significant, $r = 0.084$, $p =$ not significant, respectively). Thus, RHGS correlated with the LDL-C level and the result was shown in Figure 1.

Discussion

Recently, handgrip strength (HGS) has emerged as a substitute for muscle strength measurement owing to its convenience and economic advantages. Hence, various organizations defining sarcopenia accepted HGS as one of the most reliable tools to establish a diagnosis of sarcopenia [11–13]. However, the cutoff values of HGS defining low muscle strength differed among different studies. A review paper on sarcopenia indicated that muscle strength measured by HGS should be stratified by BMI [14]. With this data, several studies have revealed that the relative HGS adjusted for BMI (RHGS) instead of absolute HGS are inversely related to numerous age-related diseases, such as metabolic syndrome, diabetes mellitus, cardiovascular disease, and chronic kidney disease [15, 16]. In recent nationwide population-based studies, RHGS demonstrated a stronger correlation with cardiovascular biomarkers than absolute HGS and dominant HGS [17, 18]. Higher RHGS was considerably associated with a lower systolic blood pressure, TG, plasma insulin and glucose, and HDL-C levels [17].

However, any correlation between RHGS and random TG and HDL-C level was not observed in our study. Thus, our results are different from previous paper reporting that the HDL-C and TG levels were determinant factors for RHGS in the participants from the National Health and Nutrition Examination Survey [17]. Conversely, limited literature exists regarding whether RHGS correlates with the LDL-C level.

Interestingly, our study demonstrated that a positive correlation between RHGS and LDL-C level exists. However, in another previous paper, RHGS was negatively associated with LDL-C level in middle-aged and elderly community-dwelling women [10]. Compared to our results, these discrepancies may be secondary to the differently selected participants. We examined patients with T2D alone and the majority of the participants were men, accounting for 71.5%. On the other hand, the previous studies analyzed participants from National Health and Nutrition Examination Survey and middle-aged women. Also, the sample size was different from our study.

Our study has few limitations that merit consideration. First, the omission of comprehensive covariate adjustment in our analysis, including variables such as age, gender, duration of diabetes, and BMI, restricts our ability to fully account for potential confounding effects. Second, the cross-sectional design prohibits the establishment of causal relationships. Third, the analysis of nominal variables, such as gender, using traditional correlation methods presents challenges due to linearity assumptions, and while biserial cor-

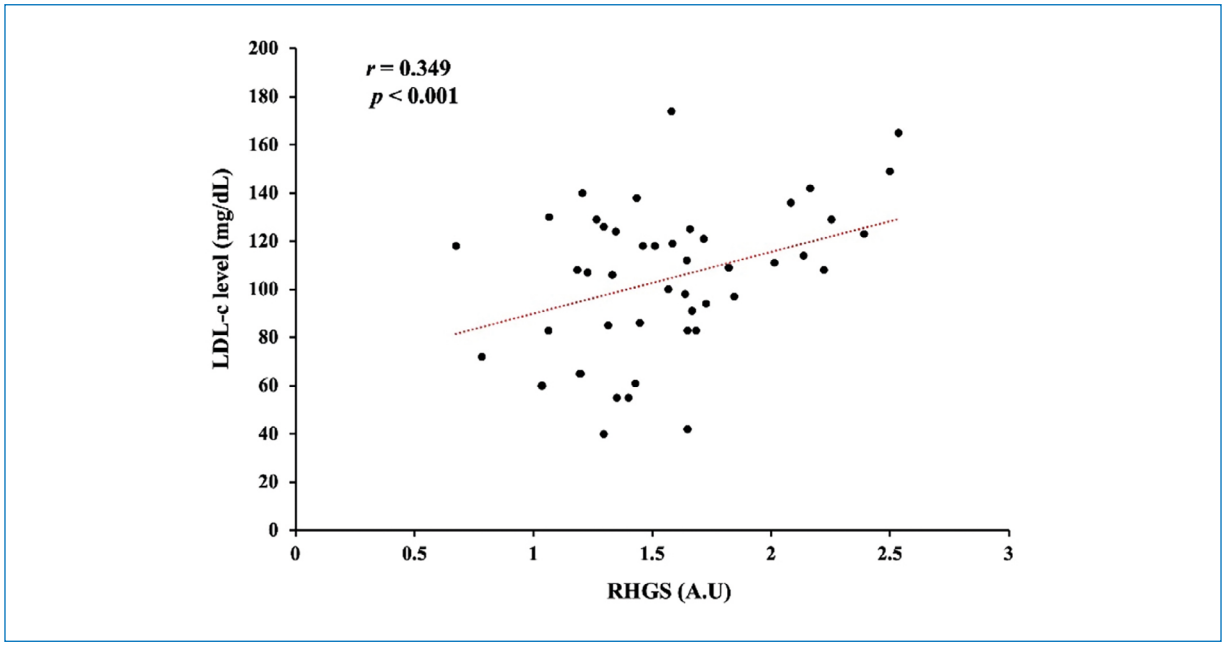

Figure 1. Regression Coefficients between the Relative Handgrip Strength (RHGS) and Low-Density Lipoprotein Cholesterol (LDL-C) Level

Regression coefficients of the univariate linear regression analysis between the RHGS and LDL-C level showed a positive correlation (r = 0.349, p < 0.001). The y- and x-axes reflect the LDL-C level and RHGS, respectively.

A.U. — arbitrary unit; LDL-C: low-density lipoprotein cholesterol; RHGS — relative handgrip strength

relation would be ideal, software constraints limited its implementation. Fourth, while our study focuses on the Japanese population, variations in socioeconomic status, cultural diversity, and healthcare access may limit the generalizability of our findings across all segments of the population. Finally, the sample size was relatively small (n = 68) and the majority of the participants were men (71.5%). Therefore, this study may be exploratory in nature without adequate power. These limitations underscore the need for cautious interpretation and highlight avenues for future research with more comprehensive datasets and study designs.

Despite these limitations, this study can suggest the following clinical implications. In the secondary prevention program of cardiovascular disease in patients with T2D, the target range of LDL-C level is below 70 mg/dL [19]. Based on our result, an extremely lower LDL-C level may cause a reduced RHGS leading to an increased risk of sarcopenia. Furthermore, as an adverse effect of cholesterol-lowering statin, an increased risk of T2D is well recognized. This adverse effect may be secondary to a reduced RHGS by cholesterol-lowering statin. When clinicians reduce the LDL-C level using a cholesterol-lowering drug, they are required to monitor the RHGS including the lipid profile to detect the early sign of sarcopenia in patients with T2D. As an extremely low LDL-C may cause a reduced RHGS leading to an increased risk of sarcopenia, clinicians are required to monitor RHGS stringently.

Article information

Data availability

The datasets generated or analyzed during this study are available from the corresponding author on reasonable request.

Ethics statement

This study complies with the guidelines for human studies in accordance with the World Medical Association Declaration of Helsinki. The subjects have signed written consent for the publication. This study protocol was reviewed and approved by the review boards of Hoshi-iin as 3-1 (March 31, 2021).

Author contributions

Shuichi Okada, Tsugumichi Saito, Tetsuro Andou, and Kihachi Ohshima designed the clinical study. Shuichi Okada and Hiroto Hoshi performed the clinical study. Kikkawa Koji, Atsushi Isoda, Junichi Okada, Kazuya Okada, Eijiro Yamada, and Shuichi Okada collected data and attended every meeting to discuss this

project. Junichi Okada, Yasuyo Nakajima, and Shuichi Okada prepared the manuscript. Shuichi Okada and Yasuyo Nakajima performed statistical analysis.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Festa A, Williams K, D'Agostino R, et al. The natural course of beta-cell function in nondiabetic and diabetic individuals: the Insulin Resistance Atherosclerosis Study. Diabetes. 2006; 55(4): 1114–1120, doi: 10.2337/diabetes.55.04.06.db05-1100, indexed in Pubmed: 16567536.
2. Sinclair AJ, Abdelhafiz AH, Rodríguez-Mañas L. Frailty and sarcopenia — newly emerging and high impact complications of diabetes. J Diabetes Complications. 2017; 31(9): 1465–1473, doi: 10.1016/j.jdiacomp.2017.05.003, indexed in Pubmed: 28669464.
3. Kimm H, Lee SW, Lee HS, et al. Associations between lipid measures and metabolic syndrome, insulin resistance and adiponectin. Usefulness of lipid ratios in Korean men and women. Circ J. 2010; 74(5): 931–937, doi: 10.1253/circj.cj-09-0571, indexed in Pubmed: 20215701.
4. Nomura T, Ikeda Y, Nakao S, et al. Muscle strength is a marker of insulin resistance in patients with type 2 diabetes: a pilot study. Endocr J. 2007; 54(5): 791–796, doi: 10.1507/endocrj.k07-055, indexed in Pubmed: 17895577.
5. Hirschler V, Maccallini G, Sanchez M, et al. Association between triglyceride to HDL-C ratio and insulin resistance in indigenous Argentinean children. Pediatr Diabetes. 2015; 16(8): 606–612, doi: 10.1111/pedi.12228, indexed in Pubmed: 25303644.
6. Ando T, Okada S, Niijima Y, et al. Impaired glucose tolerance, but not impaired fasting glucose, is a risk factor for early-stage atherosclerosis. Diabet Med. 2010; 27(12): 1430–1435, doi: 10.1111/j.1464-5491.2010.03144.x, indexed in Pubmed: 21059096.
7. Bayoumi RAL, Khamis AH, Tahlak MA, et al. Utility of oral glucose tolerance test in predicting type 2 diabetes following gestational diabetes: Towards personalized care. World J Diabetes. 2021; 12(10): 1778–1788, doi: 10.4239/wjd.v12.i10.1778, indexed in Pubmed: 34754378.
8. Cha RH, Lee GS, Yoo JuY, et al. Hand Grip and Leg Muscle Strength in Hemodialysis Patients and Its Determinants. J Korean Med Sci. 2021; 36(11): e76, doi: 10.3346/jkms.2021.36.e76, indexed in Pubmed: 33754509.
9. Hong S. Association of Relative Handgrip Strength and Metabolic Syndrome in Korean Older Adults: Korea National Health and Nutrition Examination Survey VII-1. J Obes Metab Syndr. 2019; 28(1): 53–60, doi: 10.7570/jomes.2019.28.1.53, indexed in Pubmed: 31089580.
10. Kawamoto R, Ninomiya D, Kasai Y, et al. Handgrip strength is associated with metabolic syndrome among middle-aged and elderly community-dwelling persons. Clin Exp Hypertens. 2016; 38(2): 245–251, doi: 10.3109/10641963.2015.1081232, indexed in Pubmed: 26818203.
11. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; 39(4): 412–423, doi: 10.1093/ageing/afq034, indexed in Pubmed: 20392703.
12. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014; 15(2): 95–101, doi: 10.1016/j.jamda.2013.11.025, indexed in Pubmed: 24461239.
13. Studenski SA, Peters KW, Alley DE, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci. 2014; 69(5): 547–558, doi: 10.1093/gerona/glu010, indexed in Pubmed: 24737557.
14. Chen LK, Lee WJ, Peng LN, et al. Asian Working Group for Sarcopenia. Recent Advances in Sarcopenia Research in Asia: 2016 Update From the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2016; 17(8): 767.e1–767.e7, doi: 10.1016/j.jamda.2016.05.016, indexed in Pubmed: 27372539.
15. Choquette S, Bouchard DR, Doyon CY, et al. Relative strength as a determinant of mobility in elders 67-84 years of age. a nuage study: nutrition as a determinant of successful aging. J Nutr Health Aging. 2010; 14(3): 190–195, doi: 10.1007/s12603-010-0047-4, indexed in Pubmed: 20191251.
16. Yi DW, Khang AhR, Lee HW, et al. Relative handgrip strength as a marker of metabolic syndrome: the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014-2015). Diabetes Metab Syndr Obes. 2018; 11: 227–240, doi: 10.2147/DMSO.S166875, indexed in Pubmed: 29872330.
17. Lawman HG, Troiano RP, Perna FM, et al. Associations of Relative Handgrip Strength and Cardiovascular Disease Biomarkers in U.S. Adults, 2011-2012. Am J Prev Med. 2016; 50(6): 677–683, doi: 10.1016/j.amepre.2015.10.022, indexed in Pubmed: 26689977.
18. Lee WJ, Peng LN, Chiou ST, et al. Relative Handgrip Strength Is a Simple Indicator of Cardiometabolic Risk among Middle-Aged and Older People: A Nationwide Population-Based Study in Taiwan. PLoS One. 2016; 11(8): e0160876, doi: 10.1371/journal.pone.0160876, indexed in Pubmed: 27559733.
19. Authors/Task Force Members, ESC Committee for Practice Guidelines (CPG), ESC National Cardiac Societies. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. Atherosclerosis. 2019; 290: 140–205, doi: 10.1016/j.atherosclerosis.2019.08.014, indexed in Pubmed: 31591002.