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ASSOCIATION OF HOMA-IR VALUE WITH RELATIVE HANDGRIP STRENGTH IN ADULT WOMEN IN JAKARTA

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Abstract

Muscle strength is one of the vital signs that can determine the risk of physical function and overall mortality. The rate of decline in muscle strength occurs faster than the rate of decline in muscle mass. We relate one of the factors that can influence the decrease in muscle strength to the early phase of diabetes, which is also associated with insulin resistance. We aim to determine the association between HOMA-IR value and relative hand grip strength in adult women in Jakarta. We used a cross-sectional method and obtained 68 subjects. Data were obtained through handgrip dynamometry, blood samples, 3 x 24 hours food recall, anthropometric measurements, and IPAQ-SF questionnaires. The HOMA-IR value was obtained with a median of 2.765 (0.62 - 6.12). An average of 25.32 ± 2.27 kg resulted from absolute hand grip strength. While the results of the relative handgrip strength are dividing the absolute handgrip strength by body weight, a median of 0.39 (0.22 - 0.61) was obtained. The linear regression statistical test using the Enter method showed no significant relationship between HOMA-IR and relative hand grip strength after controlling for BMI as a confounding factor.

Keywords: Relative Handgrip Strength, Homa-IR, BMI

INTRODUCTION

Muscle strength has become one of the vital signs that can determine the risk of chronic and critical illness, physical function in the elderly, quality of life, and risk of mortality.1 At first, decreased skeletal muscle strength was believed to be a direct result of reduced skeletal muscle mass. Recent evidence shows that muscle mass and strength are not linearly related.2 Decreased muscle strength (dynapenia) occurs as much as 4% per year, while decreased muscle mass (sarcopenia) occurs as much as 1% per year. This shows that factors other than muscle mass are also associated with decreased muscle strength.3 Decreased muscle strength associated with chronic hyperglycemia may occur in the early stages of diabetes. Decreased muscle strength at a younger age is associated with type 2 diabetes mellitus (DMT2) compared to the general population.4 A study compared people with T2DM and non-DM into three age groups and showed a higher increase in the prevalence of diabetes in the group with T2DM as the age group increased.5 DMT2 is the most common type of diabetes, covering 90% of all diabetes cases, and is generally characterized by insulin resistance.6 Insulin resistance is a decrease in the ability of target organs to respond to normal circulating insulin to lower blood glucose.7 The tissue insulin resistance defect is reversible with weight loss therapy and hypocaloric nutritional regimens. However, chronic overnutrition in conditions of insulin resistance can lead to a vicious cycle of hyperinsulinemia-insulin resistance, which culminates in the failure of pancreatic β-cells to excrete insulin leading to DMT2.8

One of the muscle strength tests is the hand grip strength test. This test is widely used and easy to use clinically as an indicator of general weakness with presumptive value and predictive validity, such as mortality and physical function. The validity of the handgrip strength test was also reported to be quite good compared to the manual muscle test (MMT) and several field tests.1 Absolute hand grip strength is related to body size; individuals with larger body sizes are generally stronger. When discussing aspects of muscle metabolism in clinical studies, several studies use body weight to adjust for absolute grip strength.9-11 The relative handgrip strength, the absolute handgrip strength divided by body weight, can show a stronger association with certain metabolic disorders.9

In Indonesia, based on the 2018 Riskesdas, the prevalence of T2DM in people aged ≥ 15 years was 8.5%, an increase compared to the 2013 Riskesdas, which was 6.9%. The prevalence of DMT2 is higher in women (12.7%) than in men (9.0%). DKI Jakarta is the province with the highest prevalence of DMT2 in Indonesia, with a prevalence of 2.6%, higher than the national prevalence of 1.5%.12 Women have higher insulin sensitivity than men. However, physical activity is an essential parameter for insulin sensitivity in women, where women with low physical activity can lead to an increased risk of insulin resistance.13 In developing countries like Indonesia, a shift in the type of work leads to lower physical activity levels, thereby increasing the risk of insulin resistance in women.14 Coupled with an increase in processed food products, women in developing countries have a higher opportunity to consume energy-dense non-nutritive snacks than men.15 The hyperinsulinemic-euglycemic glucose clamp (HEC) is the gold standard for determining human insulin resistance. However, HEC is challenging to implement because it requires time, money, and experienced implementers.16 One of the simpler and minimally invasive assessments of insulin resistance is the HOMA-IR15 which has a correlation of 0.6 with HEC ($p < 0.0001$).16

A study showed that the relative strength of the hand grip had a negative association with HOMA-IR in Italian Caucasian middle-aged female subjects ($p = 0.02$).17 Another study also showed that relative hand grip strength negatively correlated with HOMA-IR in normoglycemic adult males (correlation coefficient = -0.23; $p<0.001$).18 Studies on male adolescents also show that relative handgrip strength has a negative association with HOMA-IR after controlling for puberty status, country of origin, and body mass index (BMI) ($p = 0.041$).19

The above studies examined middle-aged Caucasian women and male adults and adolescents, while studies on adult women of reproductive age were still limited. Therefore, this study aims to determine the association between HOMA-IR value and relative hand grip strength and its relationship with macronutrient intake and physical activity in female subjects of reproductive age living in Jakarta, Indonesia. In addition, this research is expected to be the basis for developing further intervention-based research to improve the HOMA-IR value to increase the relative hand grip strength in adult women based on data. It is also hoped that this will serve as a basis for information on the preparation of educational materials for the subject and the public in general regarding the management of a healthy lifestyle through diet and physical activity.

RESEARCH METHODS

This study used a cross-sectional study design and is part of a large clinical trial entitled Conjugated Linoleic Acid (CLA) Combined with the Consequences of Nutrition Counseling on Body Weight and Body Fat Mass in Overweight and Obese Adults / CLAPS PROJECT Department of Nutrition and Human Nutrition Research Center (HNRC) IMERI FKUI 2020—2021.

RESULT AND DISCUSSION

Seventy subjects who contacted the researcher and signed an informed consent to be screened for Fasting blood glucose were obtained. Screening results showed that all subjects met the inclusion criteria, but two were insufficient for further blood tests. So 68 subjects were obtained, which were further analyzed.

The median age of the research subjects was 27 (18 - 49) years. As many as 79.4% of the subjects (54 people) had a higher education level. The highest proportion of subject types of work is non-manual workers, as many as 45 people (66.2%). The average BMI of the study subjects was 26.90 ± 4.85 kg/m2. Subjects with normal weight were 17 people (25%), overweight nine people (13.2%), 24 people (35.3%) included obesity category I, and 18 people (26.5%) included obesity category II. Data on the characteristics of the research subjects are shown in Table1.

Table 2. Bivariate analysis of age, BMI, nutritional status, type of work, intake of macronutrients, physical activity, and HOMA-IR on relative hand grip strength

Variables	Relative handgrip strength	P value*
Age	r=0,023	0,850
BMI	r=-0,660	< 0,001[¶]
Type of work		0,633[ǂ]
Non-manual labor	0,4049 ± 0,08338	
Manual labor	0,4067 ± 0,07891	
Student	0,3858 ± 0,10991	
Unemployment	0,3540 ± 0,11216	
Energy intake	r=0,032	0,793
Carbohydrate intake	r=-0,043	0,727
Protein intake	r=0,016	0,900
Fat intake	r=0,135	0,273
Physical activity	r=0,019	0,878
HOMA-IR	r=-0,430	< 0,001[¶]

The blood test results showed that the mean GDP was 83.19 ± 6.65 mg/dL and the median fasting blood insulin was 13.10 (3.29 - 28.83) mIU/L. The median HOMA-IR value was 2.765 (0.62 - 6.12). The absolute handgrip strength examination showed an average of 25.32 ± 2.27 kg. At the same time, the results of the relative handgrip strength by calculating the absolute handgrip strength divided by body weight obtained a median of 0.39 (0.22 - 0.61).

The median energy intake was 1718.15 (854.23 - 3035.33) kcal/day. The median carbohydrate intake was 198.705 (104.9-407.34) gram/day, the median protein intake was 56.715 (24.67 - 125.54) gram/day, and the median fat intake was 78.87 (39.64 - 169 .86) gram/day. This study found that the average fat consumption was 41.23 ± 7.83% of total daily energy. The total energy daily percentage from fat intake exceeds the FAO/WHO recommendation, which recommends the intake of the highest source of fat at 35% of total daily energy.21 This shows that the diet of the research subjects tends to be high in fat content. A study shows that the percentage of energy intake from fat has a positive association with BMI in both sexes after adjusting for energy intake from non-fat sources, physical activity, and socioeconomic status.22 The subject's physical activity through the IPAQ-SF method obtained a median of 954.5 (99 - 10290) MET-min/week. Most subjects (64.7%) underwent moderate to high physical activity.

A bivariate test was conducted to determine the relationship between the independent variables, potential confounding factors, and the dependent variable. Statistically significant results were shown by BMI and HOMA-IR values with $p < 0.001$. Other variables do not show significant results. The results of the bivariate analysis can be seen in Table 2.

Table 3 Multivariate linear regression analysis to assess the relationship between IMT and HOMA-IR with relative hand grip strength

Variables	Relative handgrip strength		
	β coefficient	CI 95%	p-value
HOMA-IR (*unadjusted*)	-0,31	-0,47-(-0,015)	<0,001
HOMA-IR (*adjusted*)	-0,009	-0,024-0,007	0,271
BMI	-0,011	-0,015-(-0,007)	<0,001

The results of multivariate analysis using linear regression with the Enter method showed no association between HOMA-IR values and relative hand grip strength after controlling for BMI as a confounding factor ($p = 0.271$). Multivariate analysis is shown in Table 3. The BMI variable was significantly a confounding factor for the relative strength of the hand grip muscles with $p <0.001$ with adjusted $R2 = 0.429$.

The results of this study are not in accordance with the study of Poggiagale et al. because it is possible that the study matched subjects in only one BMI category, so BMI was not considered a confounding factor.17 The results of this study were also inconsistent with a study where HOMA-IR had a negative correlation with RHGS ($p <0.001$; $r = -0.23$), but the subjects in the study were normoglycemic adult males.18 This study is also not in line with a study that showed HOMA-IR had a negative association with absolute hand grip strength after controlling for puberty status, country of origin, and BMI, but the study subjects were male adolescents.19

Although the mechanism linking insulin resistance and reduced muscle strength is still not fully understood, the suspected mechanism is that insulin resistance is associated with chronic low-grade inflammatory conditions.23 Adipocytes, especially adipocytes in visceral fat tissue, and macrophages secrete pro-inflammatory type-1 cytokines such as TNF-α, IL-1ß, and IFN. These cytokines can influence metabolic regulation and cause insulin resistance in various cell types, including adipocytes and skeletal muscle myocytes, through paracrine or endocrine effects. Obesity and a high-fat diet, through intramyocellular lipid content (IMCL) fatty acid metabolites, namely diacylglycerol (DAG) and cytokines, will activate protein kinase C (PKC), both conventional PKC and novel PKC, resulting in disturbances in the downstream pathways of insulin signaling leading to insulin resistance.23, 24

At another cellular level, IMCL is inversely related to muscle contractility.17 DAG and ceramides result in lipotoxicity, pro-inflammatory myokine secretion, and mitochondrial dysfunction, which leads to oxidative damage, resulting in a decrease in ATP synthesis25, as well as degradation of skeletal muscle protein, which interferes with protein turnover and muscle contractility26. Another consequence of IMCL accumulation is decreased glucose uptake into muscle cells due to impaired GLUT-4 translocation from the inside to the surface of the muscle cell membrane.27 This was shown by a study that the density of GLUT-4 on the muscle fiber surface of obese people and people with DMT2 was less than that of healthy subjects with the same muscle fiber diameter.28

Fat mass is highly correlated with BMI.29-31 Increased BMI is associated with increased intermuscular adipose tissue (IMAT). Increased pro-inflammatory cytokines characterize IMAT adjacent to muscle fibers, impaired blood flow around muscle tissue, and increased rate of lipolysis leads to insulin resistance around muscle tissue. IMAT also affects the mechanical aspects of the muscles through changes in the orientation of the muscle fibers, thereby inhibiting the production of muscle power, ultimately reducing the muscle's ability to move and function. The relationship between IMAT and BMI can theoretically be related to the relationship between IMAT and insulin resistance.3 In addition, in central obesity, IMAT correlates with visceral adipose tissue (VAT), especially in the expression of genes related to inflammatory processes, which are also associated with insulin resistance.32

Macronutrient intake in this study was obtained through interviews with 24-hour recall from three non-consecutive days. Enumerator training has been carried out to standardize intake interview techniques and anthropometric examinations. Anthropometric and handgrip examinations use validated and calibrated tools. Examination of blood serum biomarkers is carried out by professional staff in a laboratory that has national certification.

Nevertheless, this research has some limitations. The small number of subjects may cause the relationship between the dependent variable and the independent variable to be insignificant. This study used a cross-sectional design to assess the association between the HOMA-IR value and the relative strength of the hand grip at one time, so it cannot assess the causality relationship between the two variables. The method of assessing food intake through a 24-hour recall relies heavily on the subject's memory so it can lead to recall bias. One study mentions the controversy over using handgrip strength as a sign of general body strength without examining lower extremity strength.1 The HOMA-IR assessment of insulin resistance reflects hepatic insulin sensitivity because fasting plasma glucose is determined primarily by the hepatic glucose production rate (HGP), and insulin is the primary regulator of HGP. This study did not examine the oral glucose tolerance test (OGTT), which is influenced by hepatic insulin resistance and peripheral insulin resistance (mainly skeletal muscle).33 This study did not examine other factors that can affect muscle strength, such as body composition, especially fat-free mass and IMAT, as well as IMCL levels and inflammatory markers. The examination was not carried out due to limited funds and time

CONCLUSION

This study showed no association between the HOMA-IR score and the relative hand grip strength in adult women after controlling for confounding factors. BMI was significantly a confounding factor for the relative strength of the handgrip muscles. The small number of subjects may cause the relationship between the two variables to be insignificant. Further research is needed with a larger number of subjects to assess the relationship between HOMA-IR scores and relative hand grip strength to become more significant. This follow-up research can be accompanied by an examination of OGTT and lower extremity strength, as well as other factors that have not been examined that can affect muscle strength, such as body composition, IMAT, IMCL levels, and inflammatory markers. The research database is also expected to be the basis for further interventional research to improve HOMA-IR values through healthy lifestyle interventions to increase the relative hand grip strength in adult women.

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