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## Abstract of thesis

In this doctoral dissertation, MANDA Chrispin Mahala describes the new method to detect the patients in early diabetic stage. The content is summarized as follows.

### Purpose

The global prevalence of prediabetes and type 2 diabetes mellitus (T2DM) is rising rapidly. Early intervention in prediabetic individuals significantly reduces the risk of progression to T2DM. Identifying individuals at higher risk of prediabetes would therefore provide the best opportunity for the implementation of preventive strategies. Shared risk factors for non-communicable diseases (NCDs) such as obesity are well reported. However, studies from Sub-Saharan Africa (SAA) and Asia show that a substantial proportion of people with diabetes are not overweight or obese. One possible explanation might relate to the limitation of body mass index (BMI) since it lacks sensitivity for assessing disease risks, especially in people who have normal or mildly elevated body weight.

Low muscle strength has recently been suggested as another modifiable risk factor for T2DM. Therefore, the author investigated the relationship between muscle strength, body composition, and incident prediabetes among adults. This was achieved by analyzing data from

two different populations.

## **Material and method**

The first was a prospective cohort study conducted to investigate whether relative handgrip strength in adults predicted prediabetes incidence after 2 years of follow-up. The study was conducted in Ibaraki prefecture, Japan, and recruited individuals without prediabetes and diabetes attending lifestyle-related medical examinations between April 2016 and March 2017 (n = 2054). Individuals who came for the follow-up medical examinations between April 2018 and March 2019 were included in the analysis (n = 1075; women: 44.8%). Multivariable adjusted hazard ratios (aHR) of new prediabetes cases were calculated using Cox regression.

The second study was a cross-sectional study nested in a follow-up study of prediabetic and prehypertensive individuals identified during an extensive NCDs survey in Malawi which enrolled adults from two defined geographical areas within Karonga District and Lilongwe city. This study examined the relationship of handgrip strength with prediabetes and T2DM among rural and urban-dwelling adults in Malawi to assess its utility in prediabetes and T2DM screening during medical examinations. A total of 261 participants (women: 64%) were recruited between November 2018 and February 2019. Univariate and multivariate binary logistics regression analysis was performed to examine the association of prediabetes and T2DM with relative handgrip strength.

## **Results**

Findings from the first study showed that one hundred sixty-nine individuals (15.7%) developed prediabetes after a mean follow-up of 24.2 months (SD = 1.9 months). Higher baseline relative handgrip strength predicted a lower risk (aHR [95% CI] = 0.38 [0.21-0.71]) of prediabetes incidence among adults. Importantly, relative handgrip strength predicted new prediabetes cases among normal-weight individuals (aHR [95% CI] = 0.39 [0.16-0.96]). In the second study, the mean (SD) age of participants was 49.7 (13.6) years, and 54.0% were between the ages of 40 and 59 years. The mean (SD) absolute handgrip strength and relative handgrip strength were 28.8 (7.3) kg and 1.16 (0.40) kg/BMI, respectively and the mean relative handgrip strength differed significantly (P<0.001) by T2DM status. Relative handgrip strength was well correlated with anthropometric and body composition measures such as waist circumference (r=-0.510, P<0.001), hip circumference (r=-0.572, P<0.001), body fat (r=-0.501, P<0.001), muscle mass (r=-0.521, P<0.001), and muscle quality (r=0.215, P=0.037). Relative handgrip strength was associated with prediabetes and T2DM after adjusting for age (continuous), sex, place of study, hypertension, dyslipidemia, and level of education (aOR [95% CI]; 0.19 [0.03-0.95]).

## **Discussion**

The author found that lower baseline relative handgrip strength predicts a higher risk of prediabetes incidence among adults in Japan. An important finding of this study was that relative handgrip strength predicted a lower and significant risk of prediabetes incidence among individuals with normal weight (BMI 18.5-24.9 kg/m<sup>2</sup>). This study continued to demonstrate this association among participants from the urban and rural areas of Malawi, where it was found that relative handgrip strength was associated with prediabetes and type 2 diabetes mellitus. This demonstrated the utility of handgrip strength measurements among sub-Saharan Africa populations.

Relative handgrip strength was also well correlated with anthropometric, body composition measures, and cardiovascular disease biomarkers. Relative Handgrip strength measurement would, therefore, provide an opportunity for prediabetes and T2DM risk screening given the limitations of BMI.

#### **Abstract of assessment result**

##### **(General Comments)**

The author revealed that handgrip strength measurement is useful to identify individuals at high risk of newly diagnosed prediabetes, importantly, among normal weight individuals. The identified individuals may benefit from early intervention to reduce the risk of prediabetes and T2DM.

The final examination committee conducted a meeting as a final examination on Jan. 8, 2021. The applicant provided an overview of dissertation, addressed questions and comments raised during Q&A session. All of the committee members reached a final decision that the applicant has passed the final examination. The final examination committee approved that the applicant is qualified to be awarded Doctor of Philosophy in Medical Sciences.