ABSTRACT

Type 2 diabetes mellitus (DM) is commonly linked to muscle weakness and metabolic abnormalities which increase healthcare costs. The study was undertaken to investigate if low handgrip strength, as a marker of muscle weakness, is associated with hyperglycemia and/or DM in Brazilian subjects. In a cross-sectional design, 415 individuals of both sexes (46.7% male) were interviewed by a questionnaire and the DM diagnostic was self-reported. Anthropometric measurements, such as weight, height, body mass index (BMI), arm circumference, mid-arm and calf circumference and handgrip strength, were obtained by trained nutritionists. Blood glucose concentrations were determined by portable monitor analysis. Student’s t-test was applied to compare DM cases with non-diabetic individuals, and logistic regression analysis was performed to verify the odds for becoming diabetic or having altered glycemia and p < 0.05 was considered as significant. From 415 subjects, 9.2% (n = 35) were classified as DM. DM patients had significantly higher age, BMI, casual glycemia and lower handgrip strength and normalized (to body weight) handgrip strength (NHS) when compared with non-diabetic patients. Individuals with low NHS have 2.7 odds ratio to DM without adjustment for covariate (crude model, p = 0.006) and have 2.7 times higher the likelihood of DM than individuals with high NHS after adjusting for age (model 1, p = 0.006); however, this association disappeared after further adjusting for sex. In conclusion, low handgrip strength normalized or not to body weight, was not associated with hyperglycemia and DM diagnosis.

Keywords: Hand strength; Weakness; Diabetes mellitus; Blood sugar

INTRODUCTION

Type 2 diabetes mellitus (DM) is associated with an increased loss of skeletal muscle mass and its function during aging [1-5]. Though the underlying mechanisms are multifactorial, studies indicate insulin resistance, physical activity status, diet, increased secretion of inflammatory cytokines and oxidative stress may all play a role [6,7]. Screening to identify
Conflict of Interest
The authors declare that they have no competing interests.

Some evidence indicates that handgrip strength is associated with DM [3,5]. However, few statistical adjustments have been taken into account, such as sociodemographic and anthropometric variables. For example, an increase in body weight (adiposity) normally precedes the development of DM and thus research reporting an adjustment of hand grip strength to body weight is desirable. Although a Brazilian study found an association between low handgrip strength (non-normalized by body weight) and DM, this work used odds ratio (OR) analysis only adjusted by age, body mass index (BMI) and physical activity [2], and thus ignored the difference in muscle strength that exist between men and women [1,3,5,9,10]. As a result, the association between muscle weakness and DM remains to be fully explored amongst the Brazilian population. We sought to investigate if low handgrip strength is associated with the odds of becoming DM and exhibiting hyperglycemia among Brazilian individuals.

MATERIALS AND METHODS

Study population
A total of 415 (194 male and 221 female) subjects were enrolled in a cross-sectional study. Younger and older adult men and women were recruited in the first semester of 2016 from 5 public parks. The average age of the participants was 45 years (range 19–89 years). Individuals of both sexes who are recreationally active were included. We excluded the subjects who have physical or locomotive problems.

This study was approved by the Ethical Research Committee under protocol No. 1.470.285/2016. All participants signed the informed consent form designed according to the nº 466/12 on “Research involving human beings, from the Health Board of the Ministry of Health.”

Covariates
Demographic, socioeconomic, and lifestyle indicator data were collected through standard questionnaires. Body weight (kg) was obtained using an anthropometric scale (Filizola®; Filizola, São Paulo, Brazil) and height (m) using a stadiometer (SECA®; Seca GmbH, Hamburg, Germany) with BMI (kg/m²) subsequently calculated. All anthropometric measurements were performed 3 times, including arm (cm), mid-arm (cm), and calf (cm) circumferences using an inelastic tape. Handgrip strength (kg) was determined 3 times using a dominant hand trough dynamometer (Takei®; Scientific Instruments Co., Ltd., Tokyo, Japan) and classified for percentile [11]. In addition, the values were normalized to body weight (normalized handgrip strength; NHS) and classified as ‘normal’ or ‘muscle weakness’ (if below of 0.30 for females and 0.46 for males) [3,5]. All anthropometric measurements were taken by nutritionists previously trained to standardize the collection and minimize error.

Physical exercise routines were self-reported and subjects who reported no structured exercise were classified as sedentary. Thus, individuals who reported more frequent physical activity were classified as ‘recreationally active,’ among the activities more frequent were walking and jogging.
Evaluation of glycemia concentrations
Blood glucose concentrations were obtained using a finger puncture blood sample and measured using reagent strips and a portable automatic monitor (Roche®; Roche Diagnostics, Branchburg, NJ, USA). The glycemia concentrations was measured only once during the park. We considered the measurements to be ‘casual glycemia’ because the evaluation was out of clinic and not controlled for prandial state. DM diagnosis was self-reported by participants. Definition of altered casual glycemia was determined as per the criteria of the American Diabetes Association [12].

Statistical analyses
Data were represented as means and standard deviations and after Kolmogorov-Smirnov test for normality, all statistical analyses were performed. To compare non-diabetic individuals to those with DM, we applied an independent t-test. Fisher’s exact test or $\chi^2$ test was conducted to verify the difference in smoking status and alcohol intake among men and women.

Logistic regression analysis was used to calculate the OR of individual with low or normal handgrip strength and the association with DM presence or altered casual glycemia. We performed the crude (unadjusted) and adjusted (model 1: exercise frequency; model 2: age; model 3: age and sex; and model 4: age, sex, and exercise frequency) models. All statistical analyses were performed in MedCalc® (MedCalc Software, Seoul, Korea) and considered as significant when a $p < 0.05$ was found.

RESULTS
From 415 subjects, 9.2% were classified as DM. Diabetic patients showed higher ($p < 0.05$) age, BMI and casual glycemia, and lower handgrip strength and NHS when compared to non-diabetic patients (Table 1). The logistic regression analyses revealed that low NHS was associated with 2.7 times higher DM presence in crude model ($p = 0.006$) and 2.7 times after adjusting for exercise frequency (model 1, $p = 0.006$). However, this association disappeared after adjusting for sex (models 3–4, $p > 0.05$) (Table 2).

Table 1. General characteristics of non-diabetic and diabetic subjects

| Characteristics                  | Non-diabetic (n = 380) | Diabetic (n = 35) | p value |
|----------------------------------|------------------------|-------------------|---------|
| Age, yr                          | 43.99 ± 0.84           | 58.00 ± 2.49      | < 0.0001* |
| Exercise frequency, times/wk     | 1.63 ± 0.07            | 1.65 ± 0.21       | 0.470   |
| Sex, %                           |                        |                   | 0.999   |
| Male                             | 43.1                   | 3.6               |         |
| Female                           | 48.5                   | 4.8               |         |
| Smoking status, %                |                        |                   | 0.097   |
| No                               | 83.8                   | 8.3               |         |
| Yes                              | 7.7                    | 0.2               |         |
| BMI, kg/m²                       | 25.90 ± 0.22           | 27.67 ± 0.80      | < 0.0001* |
| Arm circumference, mm            | 309.80 ± 2.11          | 314.60 ± 7.39     | 0.259   |
| Mid-arm muscle circumference, mm | 237.20 ± 1.95          | 232.50 ± 5.30     | 0.244   |
| Calf circumference, cm           | 37.35 ± 0.18           | 38.77 ± 0.74      | 0.185   |
| Handgrip strength, kg            | 32.99 ± 0.52           | 27.21 ± 1.49      | 0.0008* |
| NHS†                             | 0.459 ± 0.006          | 0.380 ± 0.077     | 0.0002* |
| Casual glycemia, mg/dL           | 99.95 ± 0.93           | 167.50 ± 14.30    | < 0.0001* |

BMI, body mass index; NHS, normalized handgrip strength.
*Student’s t-test; †NHS = handgrip strength/bdy weight.
In the present study, we showed that low handgrip strength (as a measure of muscle weakness), irrespective of whether normalized to body weight, was not associated with hyperglycemia and/or the likelihood of presenting with DM once data were adjusted for age, sex, exercise frequency, and BMI. This is in line with, and extends on the findings of Leong et al. [9], who did not find any association between low handgrip strength and incidental DM in 2015.

Although there is an evidence which has pointed to a link between hyperglycemia and reduced muscle function [1], our study did not establish such a link, even in a large cohort. A possible explanation is that in our study all findings may be independent of casual glycemia concentrations. In fact, all individuals are park goers and are consequently likely performing at least a modest amount of daily physical activity. In contrast, Amaral et al. [2], also evaluated Brazilian individuals who live in both urban and rural areas of the northern region and found an association of low handgrip strength with DM in 2015. This may be because in the Amaral et al. [2], the individuals possessed a more sedentary lifestyle when compared with our study. Thus, it is suggested that more active lifestyle would lead higher handgrip strength and lower risk of DM. Another difference between the present work and the study of Amaral et al. [2] is the correction for gender. Once the handgrip values are classified according to gender, thus is possible that no correction for gender did not guarantee a direct association among low handgrip strength and DM. Besides, van der Kooi et al. [13] also suggest that ethnic differences may to explain the loss of handgrip strength. Therefore, we speculate that the discrepancies seen in previous studies are better explained by these independent risk factors, rather than hyperglycemia or DM per se.

This study has some limitations. First, the cross-sectional design of the study does not allow a generalization of data to infer causality between muscle weakness and DM, rather, only an association can be established. Second, the casual glycemia was performed in public parks on the weekends, which may introduce substantial variation associated with physical activity status, prandial status, etc.

In summary, low handgrip strength (muscle weakness) normalized or not to body weight, was not associated with self-reported DM diagnosis or altered casual glycemia concentrations after adjusted for age, gender, and exercise frequency.

### Table 2. Associations of handgrip strength with type 2 DM and hyperglycemia

| Variables               | Crude          | Model 1          | Model 2          | Model 3          | Model 4          |
|------------------------|----------------|------------------|------------------|------------------|------------------|
| Type 2 DM              |                |                  |                  |                  |                  |
| Handgrip strength*     | 2.04 (0.79–5.25) | 2.05 (0.79–5.30) | 2.25 (0.83–6.06) | 2.13 (0.78–5.78) | 2.10 (0.77–5.73) |
| NHS†                   | 2.72 (1.32–5.58) | 2.71 (1.32–5.57) | 1.59 (0.74–3.44) | 1.88 (0.83–4.01) | 1.82 (0.83–4.01) |
| Altered casual glycemia‡ | 1.00 (0.99–1.01) | 1.00 (0.99–1.01) | 1.00 (0.99–1.01) | 1.00 (0.99–1.01) | 1.00 (0.99–1.01) |

Data shown are odds ratio (95% confidence interval). Details of each model are follow as: model 1, adjusted by exercise frequency (times/week); model 2, adjusted by age; model 3, adjusted by age and sex; and model 4, adjusted by age, sex, and exercise frequency.

DM, diabetes mellitus; NHS, normalized handgrip strength.

*Handgrip strength is low (muscle weakness) (normal: ≥ p10 or muscle weakness: < p10); †NHS (handgrip strength/body weight, male: < 0.46 or female: < 0.30) is low muscle weakness; ‡Altered casual glycemia was classified when > 200 mg/dL was found; §p < 0.05.
ACKNOWLEDGEMENTS

We would like to thank all the participants and the City Hall of Goiânia for release the data collection in the public parks.

REFERENCES

1. Kalyani RR, Kim C, Ferrucci L, Laughlin GA, Kritz-Silverstein D, Kong S, Nan B, Barrett-Connor E. Sex differences in the association of fasting and postchallenge glucose levels with grip strength among older adults: the Rancho Bernardo Study. BMJ Open Diabetes Res Care 2015;3:e000086.
2. Amaral Cde A, Portela MC, Muniz PT, Farias Edos S, Araújo TS, Souza OF. Association of handgrip strength with self-reported diseases in adults in Rio Branco, Acre State, Brazil: a population-based study. Cad Saude Publica 2015;31:1313-25.
3. Peterson MD, McGrath R, Zhang P, Markides KS, Al Snih S, Wong R. Muscle weakness is associated with diabetes in older mexicans: the Mexican health and aging study. J Am Med Dir Assoc 2016;17:933-8.
4. Li JJ, Wittert GA, Vincent A, Atlantis E, Shi Z, Appleton SL, Hill CL, Jenkins Al, Januszewski AS, Adams RJ. Muscle grip strength predicts incident type 2 diabetes: population-based cohort study. Metabolism 2016;65:883-92.
5. McGrath R, Vincent BM, Al Snih S, Markides KS, Peterson MD. The association between muscle weakness and incident diabetes in older Mexican Americans. J Am Med Dir Assoc 2017;18:452.e7-452.e12.
6. Howard C, Ferrucci L, Sun K, Fried LP, Walston J, Varadhan R, Guralnik JM, Semba RD. Oxidative protein damage is associated with poor grip strength among older women living in the community. J Appl Physiol (1985) 2007;103:17-20.
7. Park SW, Goodpaster BH, Lee JS, Kuller LH, Boudreau R, de Rekeneire N, Harris TB, Kritchevsky S, Tylavsky FA, Nevitt M, Cho FW, Newman ABHealth, Aging, and Body Composition Study. Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. Diabetes Care 2009;32:1993-7.
8. Peterson MD, Zhang P, Choksi P, Markides KS, Al Snih S. Muscle weakness thresholds for prediction of diabetes in adults. Sports Med 2016;46:619-28.
9. Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, Seron P, Ahmed SH, Rosengren A, Kiat S, Rahman O, Swanepoel D, Colder NH, Feresu S, Gotey D, Pokharel G, Verma A, Ponczok J, Zhang T, Vlček P, Varga J, Paltola M, Double WH, CARDIA, The Multi-Ethnic Study of Atherosclerosis (MESA) Investigator Group. Ambulatory blood pressure monitoring and risk of type 2 diabetes: the Multi-Ethnic Study of Atherosclerosis (MESA) study. PLoS One 2012;7:e38936.
10. Mainous AG 3rd, Tanner RJ, Anton SD, Jo A. Low grip strength and prediabetes in normal-weight adults. J Am Board Fam Med 2016;29:280-2.
11. Schlüssel MM, dos Anjos LA, de Vasconcellos MT, Kac G. Reference values of handgrip dynamometry of healthy adults: a population-based study. Clin Nutr 2008;27:604-7.
12. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2018. Diabetes Care 2018;41:S13-27.
13. van der Kooi AL, Snijder MB, Peters RJ, van Valkengoed IG. The association of handgrip strength and type 2 diabetes mellitus in six ethnic groups: an analysis of the HELIUS study. PLoS One 2015;10:e0137739.