METABOLISM CLINICAL AND EXPERIMENTAL 65 (2016) 883–892

Available online at www.sciencedirect.com

Metabolism

www.metabolismjournal.com

Muscle grip strength predicts incident type 2 diabetes: Population-based cohort study

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ARTICLE INFO

Article history:
Received 11 February 2016
Accepted 22 March 2016

Keywords:
Skeletal muscle
Lean mass
Dual energy X-ray absorptiometry
Muscle strength
Grip strength

ABSTRACT

Objectives. To determine the longitudinal relationship of muscle mass and strength with incident type 2 diabetes, and previously unstudied mediating effects of testosterone and inflammation.

Methods. Community-dwelling male participants (aged ≥35 years) of the Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study underwent biomedical assessment in 2002–2006 and 2007–2010, including hand grip strength (dynamometer), testosterone and inflammatory markers. Body composition (dual-energy X-ray absorptiometry) was assessed at baseline only. Incident type 2 diabetes was defined as a self-reported doctor diagnosis, diabetes medication use, fasting plasma glucose ≥7.0 mmol/L, or glycated haemoglobin ≥6.5% (48 mmol/mol) at follow-up, that was not present at baseline.

Results. Of n = 1632 men, incident type 2 diabetes occurred in 146 (8.9%). Muscle mass was not associated with incident type 2 diabetes. Grip strength was inversely associated with incident type 2 diabetes [unadjusted odds ratio (OR) per 5 kg: 0.87, 95% confidence interval (CI): 0.80–0.95; adjusted OR, 95% CI: 0.87, 0.78–0.97]. Arm muscle quality (grip strength divided by arm lean mass) was similarly associated with incident type 2 diabetes. Testosterone, IL-6 and TNF-α did not significantly mediate the associations. The population attributable fraction of type 2 diabetes from low grip strength was 27% (13–40%), assuming intervention could increase strength by 25%.

Conclusions. Reduced muscle strength, but not reduced muscle mass, is a risk factor for incident type 2 diabetes in men. This is not mediated by testosterone or inflammation. Intervention could prevent a substantial proportion of disease.

Abbreviations: ASM, appendicular skeletal muscle mass; ASMI, appendicular skeletal muscle mass index; DXA, dual-energy xray absorptiometry; FAMAS, Florey Adelaide Male Ageing Study; FMI, fat mass index; MAILES, Men Androgen Inflammation Lifestyle Environment and Stress; NWAHS, North West Adelaide Health Study; MET, metabolic equivalent; PAF, population attributable fraction.

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http://dx.doi.org/10.1016/j.metabol.2016.03.011
0026-0495/

1. Introduction

The prevalence of type 2 diabetes has been increasing worldwide [1], in association with rising obesity. However, increased adiposity contributes to only 37–77% of incident type 2 diabetes, depending on the population studied [2,3]. Thus, identification of new and potentially modifiable risk factors is needed to inform strategies for prevention.

Multiple cross-sectional studies have shown type 2 diabetes is inversely associated with skeletal muscle mass [4,5] and strength [6,7]. Muscle strength is also inversely associated with the development of insulin resistance [8]. However, there are few longitudinal studies that have investigated the role of muscle mass and strength in the development of type 2 diabetes. Only three longitudinal studies have investigated muscle strength and incident type 2 diabetes, and they showed conflicting results which may due to methodological limitations from an inability to identify undiagnosed cases [9–11]. Furthermore, only one previous study has investigated muscle mass and incident type 2 diabetes, which found that changes in muscle mass did not predict incident type 2 diabetes [12]. However, that study relied on bioelectrical impedance analysis instead of gold standard measures such as dual-energy X-ray absorptiometry (DXA) [12]. The association between reduced skeletal muscle mass or strength and incident type 2 diabetes is therefore unclear.

Testosterone is a determinant of muscle mass and strength [13], and low testosterone has also been associated with type 2 diabetes in men [14]. Therefore low testosterone may mediate the association between skeletal muscle dysfunction and type 2 diabetes in men. Similarly, inflammation predicts decline in skeletal muscle mass and strength [15], while also predicting incident type 2 diabetes [16]. Hence inflammation may also mediate any association between skeletal muscle and incident type 2 diabetes. These mechanisms have not been previously explored.

We therefore aimed to investigate the association between measures of skeletal muscle mass and strength with incident type 2 diabetes in a prospective community-dwelling cohort of men, and whether testosterone or inflammation mediates that association.

2. Methods

2.1. Cohort participants

The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) study is a longitudinal cohort of community-dwelling men, and has been described previously [17]. In brief, MAILES consists of two concurrent prospective cohorts: the Florey Adelaide Male Ageing Study (FAMAS) [18] and the age-matched men from the North West Adelaide Health Study (NWAHS) [19]. The two cohorts are largely representative of the male population of South Australia, and used the same methodology for random population sampling.

Detailed demographic, comorbidity (doctor diagnosed diabetes, cardiovascular disease), hand dominance, and risk factor data (smoking, physical activity) were collected by self-completed questionnaire. Biomedical assessments at baseline and follow-up were conducted in 2 hospital-based clinics using standardised and reproducible study protocols, including grip strength and blood pressure measurement, anthropometry, and fasting blood samples (lipids, glucose, glycated hemoglobin, testosterone and inflammatory markers). Hypertension was defined as any of: self-report, a clinically measured systolic blood pressure of ≥140 mmHg (mean of two or three readings), diastolic blood pressure of ≥90 mmHg (mean of two or three readings), or use of anti-hypertensive medication. Metabolic syndrome was defined by International Diabetes Federation criteria. Mild (walking), moderate, and vigorous physical activity levels were determined by the Australian National Health Survey Physical Activity instrument and converted into metabolic equivalents (METs). In the NWAHS, depression was defined as a score of ≥21 on the Center for Epidemiological Studies Depression Scale, whereas in FAMAS, depression was defined as a score of ≥12 on the Beck Depression Inventory. Cardiovascular disease was defined as a self-report of doctor-diagnosed myocardial infarction, angina, stroke or transient ischemic attack.

Approval for MAILES was obtained from the Human Research Ethics Committees of the North West Adelaide Health Service and the Royal Adelaide Hospital. All participants gave written informed consent. Baseline data were obtained in 2002–2006 and follow-up data in 2007–2010. Fig. 1 shows the participant flowchart. Almost all (96%) participants were born in Australia or Western Europe (including the UK/Ireland).

2.2. Skeletal muscle measures

Grip strength was measured with a Jamar analog hand dynamometer in the NWAHS cohort (Lafayette Instrument Company, Lafayette, IN) or a Smedley analog hand dynamometer (Stoelting Corporation, Wood Dale, IL) in the FAMAS cohort [17]. To account for any systematic differences in the type of hand dynamometer used, we included cohort as a covariate in adjusted statistical analyses. Main analyses used the mean of three measurements in the dominant hand. Sensitivity analyses used the maximum (i.e. peak) measurement recorded in either hand. We also undertook sensitivity analyses to account for: 1) bodily (e.g. hand) pain, as determined by the bodily pain scale of the SF-36; 2) self-reported current smoking at baseline; and 3) use of systemic corticosteroids at follow-up.

Body composition was measured at baseline in a sub-set of the cohort (n = 1181): NWAHS participants aged ≥50 years [20], and all FAMAS participants [18]. Whole-body, arms, and legs lean mass and fat mass were measured by DXA using default settings on either a pencil-beam (DPX+, Lunar software v4·7e) or fan-beam (Prodigy DF+ 14759, Encore software v9·15) densitometer. Both machines were from GE Lunar (Madison, WI) and provided similar results [21]. Appendicular skeletal muscle mass (ASM) was calculated by summing the lean mass of arms and legs. ASM and fat mass were normalised for height by dividing by height squared to generate ASM index (ASMI), and fat mass index (FMI), respectively [20,22].

Arm muscle quality (grip strength corrected for arm lean mass) was calculated by dividing the sum of the grip strength in both hands by arms lean mass [23,24]. Sensitivity analyses were also undertaken using arm muscle quality calculated with peak grip strength.