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# **Cut-Points of Muscle Strength Associated with Metabolic Syndrome in Men**

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# **Abstract**

**Introduction—**The loss of muscle strength with age increases the likelihood of chronic conditions including metabolic syndrome (MetS). However, the minimal threshold of muscle strength at which the risk for MetS increases has never been established.

**Objective—**To identify a threshold of muscle strength associated with MetS in men.

**Methods—**We created receiver operating curves for muscle strength and the risk of MetS from a cross-sectional sample of  $5685$  men aged  $< 50$  years and  $1541$  men aged  $\leq 50$  years enrolled in the Aerobics Center Longitudinal Study. The primary outcome measure, the MetS was defined according to the NCEP ATPIII criteria. Upper and lower body muscle strength was treated as a composite measure of 1 repetition maximum tests on bench and leg press and scaled to body weight. Low muscle strength was defined as the lowest age-specific 20<sup>th</sup> percentile while high muscle strength was defined as composite muscle strength above the 20<sup>th</sup> percentile.

**Results—**In men aged < 50 years, the odds of MetS were 2.20 fold (95%CI: 1.89–2.54) higher in those with low muscle strength, independent of age, smoking, and alcohol intake. The strength of this association was similar for men aged  $\,$  50 years (OR: 2.11, 95%CI: 1.62–2.74). In men aged

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 $<$  50 years, the threshold of muscle strength associated with MetS was 2.57 kg/kg body weight, while in men aged 50 years this threshold was 2.35 kg/kg body weight.

**Conclusion—This study is the first to identify a threshold of muscle strength associated with an** increased likelihood of MetS in men. Measures of muscle strength may help identify men at risk of chronic disease.

#### **Keywords**

Dynapenia; Sarcopenia; Metabolic health; Muscular strength; Insulin resistance syndrome; Syndrome X

# **INTRODUCTION**

In sedentary individuals, muscle mass and strength decrease progressively after the age of 20 years (5,10) with a peak loss observed around 65 years of age (5,10,26). While sarcopenia is a well-established consequence of aging (5), the loss of muscle strength appears to be a more robust determinant of age-related morbidity (7,11). For example, impaired physical function is increased 2-fold in individuals with low muscle strength but only 1.4-fold among individuals with low muscle mass (24). In addition to loss of function, low muscle strength is a predictor of type 2 diabetes (29), cardiovascular morbidity and mortality, and quality of life (25,27,29,36). The mechanisms underlying the association between muscle strength with health outcomes in older individuals remain unclear, however they may be attributed to a propensity for cardiometabolic risk factor clustering.

Metabolic syndrome is a clustering of risk factors associated with type 2 diabetes and cardiovascular disease (17) characterized by a state of insulin resistance (18). Metabolic syndrome is more prevalent in men (9) and older individuals, (9) and is associated with several modifiable lifestyle factors, including physical activity levels (20), cardiorespiratory fitness (8,16), and muscle strength (38). Our group previously reported that the prevalence and incidence of the metabolic syndrome increase in a dose-response manner with decreasing muscle strength in middle-aged men (15,16). However, the threshold of muscle strength needed to prevent metabolic syndrome with aging remains unclear.

In light of these limitations in the literature, we performed a cross-sectional analysis of the Aerobics Center Longitudinal Study (ACLS) data in men aged between 20–100 years aiming at identifying minimal threshold of muscle strength associated with the presence of metabolic syndrome. A secondary aim of the study was to determine if this association was more robust in men older than 50 years, as previous studies by our group suggest that the association between strength and metabolic syndrome may be modified by age. Analyses were restricted to men, as the metabolic syndrome is more common among men, thereby increasing the statistical power to detect and association.

## **METHODS**

#### **Participants**

Between 1981 and 1989, 7393 men aged between 20 and 100 years participated in the ACLS and provided a valid assessment of upper and lower body muscle strength. Among these men, 113 had established cardiovascular disease or stroke prior to testing and were excluded for the analysis while 54 were excluded because of an established diagnosis of cancer. Therefore, 7,226 participants were included in the final analysis. No differences in age  $(42.0 \pm 9.5 \text{ vs. } 45.8 \pm 9.8 \text{ years})$ , body mass index  $(26.0 \pm 3.4 \text{ vs. } 26.8 \pm 3.8 \text{ kg/m}^2)$ , or cardiorespiratory fitness ( $12.4 \pm 2.5$  vs.  $12.0 \pm 2.4$  METs) were noted between individuals excluded from the analysis and those that remained in the analysis. The Cooper Institute institutional review board approved the study protocol, and all participants read the consent form and provided written informed consent before data collection.

#### **Outcome measure**

The primary outcome measure was metabolic syndrome, defined according to the NCEP ATPIII criteria (1) as meeting three or more of the following criteria: abdominal obesity (waist girth >102 cm), high serum triglycerides (≥150 mg/dl), low high-density lipoprotein (HDL)-Cholesterol (< 40 mg/dl), high blood pressure (BP) ( $\,$  130 mmHg systolic or  $\,$  85 mmHg diastolic or self-reported hypertension), and high fasting glucose ( $\pm 100$  mg/dl) or self-reported diabetes). All participants completed a medical history questionnaire, which included personal and family health history, smoking habits, and alcohol intake.

**Cardiometabolic Profiles—**Resting blood pressure was measured manually with a mercury sphygmomanometer in a sitting position. Two measures separated by 2 minutes were taken after the participants were sitting for at least 5 minutes. A third measure was taken and averaged if the two measures differed by more than 5 mmHg. Following a 12 hour fast, serum triglycerides, HDL-cholesterol, and plasma glucose were sampled and assayed with automated techniques. The laboratory meets the quality control standards of the U.S. Centers for Disease Control and Prevention Lipid Standardization Program.

#### **Primary exposure variable**

**Muscle strength—**Muscle strength was assessed from a standardized strength assessment protocol using variable-resistance Universal weight machines (Universal Equipment, Cedar Rapids, IA) (2). Upper and lower body strength was assessed with a one-repetition maximum (1-RM) supine bench press and seated leg press. Initial loads were set at 70 and 100% of body weight for the bench and leg press, respectively. Thereafter, load was increased by 2.27–4.54 kg (5–10 lbs) until maximal effort was achieved for both bench and leg press. 1-RM bench press and leg press were expressed by kilograms of weight lifted divided per kilogram of body weight as suggested by the American College of Sports Medicine (2). Other validated and precise methods of reporting muscle strength could have been used (i.e. allometric scaling), however the 1-RM was expressed relative to body weight to facilitate translation of study findings into a practical setting. Finally, a composite of muscle strength was calculated by combining the relative 1-RM for the bench and leg press. We have previously documented a strong intra-class correlation for the 1-RM bench press

and leg press (15) suggesting an acceptable reliability and supported the use of the composite measure.

#### **Confounding variables**

**Anthropometric measures—**Height and body weight were measured with a standard stadiometer and physician's scale at the nearest 0.1 cm and 0.1 kg respectively. Body mass index (BMI) was computed from measured height and weight with the following formula: weight (kg)/height ( $m<sup>2</sup>$ ). Waist circumference was measured at the umbilicus between the iliac crest and the last lower ribs with an anthropometric tape at the nearest 0.1 cm.

**Cardiorespiratory Fitness—**Cardiorespiratory fitness was determined with a graded maximal treadmill test to exhaustion using a modified Balke protocol as previously described (6). Participants began walking at 3.3 mph without an incline for 1 minute. The treadmill grade was increased by 2% after the first minute and 1% every minute thereafter. When the participants reached 25 minutes, the elevation was maintained at 25% and the speed was increased by 0.2 mph every minute until exhaustion of the participants or if the physician stopped the test for medical reasons. Maximal metabolic equivalent of task (METs) were calculated from the total treadmill time using an age-specific formula (1.44 x (time, min)  $+ 14.99$ ) / 3.5 to estimate maximal oxygen uptake (31).

**Physical activity—**Leisure-time physical activity was self-reported with a validated health habits questionnaire (28) and estimated from a recollection of activities in the previous three months. Participant physical activity levels were stratified into one of three categories. Those reporting no exercise in the previous 3 months were given a score of 0 and were considered sedentary. Those who participated in sports, leisure-time physical activity, or walked, jogged, or ran  $10$  miles per week were given a number of 1 and were categorized as moderately active. Participants who walked, jog, or ran >10 miles per week were given a number of three and considered as vigorously active.

**Smoking status and alcohol intake—Participants were questioned about their smoking** status and were categorized into categories: never smoked, former smoker, and current smoker, while alcohol consumption was reported in number of drinks per week.

#### **Statistical analyses**

Continuous and categorical variables are presented as means  $\pm$  standard deviations and n (%) respectively. Muscle strength measured by bench press or leg press was reported relative to body weight in kilograms. Muscle strength was also treated as a binary outcome and low muscle strength was defined according to age-specific criteria established by the American College Sports Medicine (ACSM) (2). Specifically, 1-RM values below the 20<sup>th</sup> percentile for an individual's age was classified as low muscle strength. Considering there is no age-specific cut-point from the ACSM for the composite strength, men below the 20<sup>th</sup> percentile for both tests were classified as low muscle strength as harmonizing the stratification with the ACSM criteria would facilitate the integration of study results into a practical setting. We tested for an interaction between muscle strength and age since participants in our sample are aged between 20 and 100 years. The interaction was

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significant (P=0.008) and therefore, analyses were run separately for men older and younger than 50 years. We selected 50 years as a cut-point since only 4.1% of the sample were aged over 60 years and previous studies by our group reveal that stratifying the cohort at age 50yrs provides adequate power to test for differences in metabolic syndrome between men categorized by modifiable lifestyle behaviors (35).

The following formula ( $z^2 = P(1-P)/m^2$ ) was used to determine the power available to detect differences in the prevalence of metabolic syndrome between two groups in this sample. Assuming a sample size of 1175 in men aged < 50yrs in the low muscle strength group and a sample of 4510 in the high muscle strength group, we had 99% power to detect a difference of 13% in the metabolic syndrome using a Chi-square test.

Independent T-tests, Chi-square tests or Fisher exact tests when appropriate were performed to identify differences between high and low muscle strength in men. Logistic regression analyses were performed to investigate the association between low muscle strength and metabolic syndrome in men after adjustment for confounding variables. Finally, Receiver Operating Characteristics (ROC) curves were created to quantify sensitivity, specificity, area under the curve, and threshold of muscle strength associated with the metabolic syndrome. Analyses were adjusted for age, drinking, smoking status, cardiorespiratory fitness, and body mass index. For all statistical tests, P value 0.05 at 2-tailed was considered significant. Statistical analysis was performed with SAS version 9.2 (SAS Institute Inc, Cary, NC).

# **RESULTS**

#### **Descriptive characteristics**

Among the 7226 men included in the final analysis, 27% were over 50 years of age (mean age  $55.6 \pm 5.4$  years), and, 23% displayed the metabolic syndrome.

#### **Comparison of baseline characteristics between young and older men**

Baseline characteristics of participants stratified by age group are presented in Table 1. Compared to older men, young men displayed lower waist circumference  $(92.2 \pm 10.3 \text{ cm})$ vs. 94.9  $\pm$  9.5 cm; P<0.01) and body mass index (25.8  $\pm$  3.5 kg/m<sup>2</sup> vs. 26.2 3.1 kg/m<sup>2</sup>; P<0.01). As for the metabolic profile, young men displayed lower fasting triglycerides  $(125.6 \pm 88.9 \text{ mg/dl vs. } 143.3 \pm 97.9 \text{ mg/dl; } P < 0.01)$ , glucose  $(99.0 \pm 12.2 \text{ mg/dl vs. } 104.0 \pm 10.0 \text{ m})$ 19.3 mg/dl; P<0.01), and systolic blood pressure (117.67 $\pm$  11.6 mmHg vs. 123.3  $\pm$  14.8 mmHg; P<0.01). The proportion of men with the metabolic syndrome was lower in young men compared to older men (20.7 vs. 31.6%; P<0.01).

### **Comparisons of exposure variables between low and moderate-high muscle strength stratified by age group**

Participant characteristics stratified according to muscle strength are presented in Table 2. Among men <50 years, individuals with low muscle strength displayed a higher body mass index (27.4  $\pm$  4.3 kg/m<sup>2</sup> vs. 25.4  $\pm$  3.1 kg/m<sup>2</sup>; P<0.01), fasting triglycerides (143.7  $\pm$  95.1 mg/dl vs. 121.1 86.7 mg/dl; P<0.01), fasting glucose (101.5  $\pm$  16.2 mg/dl vs. 98.4  $\pm$  10.9

mg/dl; P<0.01), and systolic and diastolic blood pressure (systolic:  $119.3 \pm 12.0$  mmHg vs. 117.4  $\pm$  11.5 mmHg, diastolic 80.4  $\pm$  9.3 mmHg vs. 78.1  $\pm$  8.8 mmHg; P<0.01), compared to those with moderate-high muscle strength. The proportion of participants having the metabolic syndrome was ~ 2-fold higher in men with low muscle strength (33.4% vs. 17.4%, P<0.01). Individuals with low muscle strength also had lower cardiorespiratory fitness compared with men with moderate-high muscle strength (11.3  $\pm$  2.1 METs vs. 13.0  $\pm$ 2.4 METs; P<0.01). Similar results were observed in men aged 50 years.

#### **Association between low muscle strength and metabolic syndrome in men**

Table 3 presents the results of logistic regression analyses testing for differences in metabolic syndrome between the age groups after adjusting for confounding variables. In men aged <50 years, independent of age, smoking, and alcohol intake the odds of metabolic syndrome were 2.20-fold (95%CI: 1.90–2.54) greater in men with low muscle strength. This association remained significant after adjusting for body mass index (1.29 95%CI: 1.10– 1.53) and cardiorespiratory fitness alone (1.23 95%CI: 1.05–1.45). However, this association disappears when both variables were added simultaneously in the model  $(P>0.05)$ .

In participants aged 50 years, independent of age, smoking, and alcohol intake, the odds of metabolic syndrome were 2.11-fold (95%CI: 1.62–2.74) higher in men with low composite muscle strength. This association was no longer significant after adjusting for body mass index.

# **Threshold of muscle strength associated with metabolic syndrome stratified by age group in men**

In men aged <50 years, independent of age, smoking, alcohol intake, and body mass index, the adjusted lower limit of muscle strength associated with a reduced odds of the metabolic syndrome was 2.56 kg/kg of body weight. The corresponding sensitivity and specificity for predicting the metabolic syndrome was 75.7 and 71.0.

In men  $\,$  50 years, independent of age, smoking, alcohol intake, and body mass index, the adjusted lower limit of muscle strength associated with a lower odds of the metabolic syndrome was 2.50 kg/kg of body weight. The corresponding sensitivity and specificity for predicting metabolic syndrome according was 73.0 and 64.3 respectively (Table 4).

#### **DISCUSSION**

The current analysis supports the concept that muscle strength is an important determinant of health outcomes in men and provides several novel findings that are relevant to the prevention of cardiometabolic diseases among men. First, similar to previous studies, we found that men with low muscle strength are more likely to display the metabolic syndrome, independent of age, BMI or cardiorespiratory fitness. Second, we found that the cardiometabolic consequences of low muscle strength are more significant among men < 50 years of age than in older men. Finally, we have defined thresholds of muscle strength that are associated with a significantly increased risk of metabolic syndrome. Collectively, these

data reinforce the importance of muscle strength as a modifiable determinant of cardiometabolic risk in men and provide targets for practitioners.

Loss of muscle strength is emerging as an independent determinant of health outcomes, especially among older individuals (34). The results presented here support previous work demonstrating that low muscle strength is associated with metabolic syndrome (34). Interestingly, we found that this association is particularly evident in men less than 50 years of age. This result is surprising considering that metabolic syndrome is more common among older individuals (9) and muscle strength decreases significantly with aging (5,10,26). Previous studies have shown that handgrip strength is associated with cardiometabolic risk (34,40) and mortality (22). The results presented here extend these findings by demonstrating that overall muscle strength is associated with metabolic syndrome, which is not trivial, as a composite measure of lower and upper body strength is a better predictor of health than handgrip strength (22). Furthermore, studies performed in older population failed to control for important confounding variables. The current study overcomes these limitations as we adjusted for adiposity and fitness to investigate the relationship between muscle strength measured by common exercises in a large population of men. The results presented here suggest that men with muscle strength below the 20th percentile for age are at a greater risk for the metabolic syndrome especially in young men.

Muscle strength thresholds have been identified for measures of low cardiorespiratory fitness (3), insulinemic profile (4), independence (30,33) and activities of daily living in older individuals (12). Very few studies have identified a threshold of muscle strength associated with health outcomes in adults (3,4,39) in particular, the metabolic syndrome (39). Wilkerson et al. (2010) (39), found that leg muscle strength < 2.93 Nm/kg was associated with an increase likelihood of metabolic syndrome, however, they failed to adjust for cardiorespiratory fitness. In our study, we found that a composite strength  $\lt$  2.86 kg/kg of body weight was associated with the presence of metabolic syndrome in men aged < 50 years independent of cardiorespiratory fitness. The sensitivity and specificity observed for this threshold were 74.3 and 66.9 respectively, while in the study performed by Wilkerson et al. (2010) (39), the sensitivity and the specificity of this muscle strength threshold were 92.0 and 64.0 respectively. The lower sensitivity and specificity reported in our study might be related to differences in age (38 vs. 19 years), cardiorespiratory fitness levels of the populations studied (43 vs. 30 ml/kg/min), the methods used to assess muscle strength (biodex vs. leg and bench press) as well as the use of a composite measure of muscle strength in the model (23). The data presented in the current study extend these observations by delineating thresholds of muscle strength for commonly used exercises that are associated with chronic disease risk in independent men. The data reinforce the concept that muscle strength may be an important modifiable lifestyle factor for cardiometabolic disease risk assessment, similar to physical activity, cardiorespiratory fitness and healthy dietary patterns (19,32).

Recent experimental trials of resistance training support observational studies by demonstrating that increasing muscle strength improves cardiometabolic risk profiles (37). In fact, several resistance training trials have demonstrated clinically relevant improvements in glycemic control and blood pressure in adults with the metabolic syndrome (38) and type

2 diabetes (21). These effects appear to be related in part to gains in muscle strength rather than changes in muscle mass (13,14) and are comparable to improvements seen with aerobic exercise alone. The data presented here support these findings and highlight the importance of muscle strength for achieving health benefits in men < 50 years of age.

The strength of this study includes a large sample size, two commonly used exercises of muscle strength, and a broad age range. Despite these strengths, there are some limitations that need to be highlighted. First, the test of muscle strength used was performed in relatively healthy individuals, without cardiovascular disease. Therefore, the generalization of our results is limited to healthy younger and older men. Second, the thresholds proposed by the current study were developed from measurements made on Universal fitness equipment. Therefore the thresholds identified may not be generalizable to other devices such as free weights that are commonly used for training and measurement. Third, the stratification of the cohort at age 50 was based on power and therefore may not reflect the age at which the association between muscle strength and metabolic syndrome become more robust. Fourth, while we were able to adjust for several confounding variables, we were unable to adjust for medication use and the level of hydration, which may impact muscle strength and therefore, could have influenced study results. Finally, due to the crosssectional nature of the study design, we are unable to draw conclusions regarding the causality of the associations observed.

In summary, we found that low muscle strength is associated with an increased likelihood of metabolic syndrome, particularly among men < 50 years of age. A threshold of muscle strength also exists that may help practitioners (i.e. exercise physiologists) identify high risk patients or serve as targets for exercise training programs designed to reduce the risk of metabolic syndrome in men. Future studies should examine the temporal nature the association between thresholds of muscle strength and metabolic syndrome and/or determine if increasing muscle strength in older men reduces the likelihood of metabolic syndrome.

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#### **Table 1**

#### Participant characteristics



Continuous variables are presented as mean ± standard deviation and categorical variables are presented as n (%). Relative muscle strength is defined as muscle strength (kg) divided by body mass (kg). BMI= Body mass index, HDL-cholesterol= High density lipoproteins



 $0.01$ 

 $0.62$ 

 $0.10\,$ 

 $0.72$ 

 $0.01$ 

 $0.16$  $0.48$ 

0.32

 $0.24$ 

 $0.01$ 

 $<0.01$ 

 $<0.01$ 

0.18  $0.58\,$   $0.01$ 

 $0.71$ 

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**P** value  $0.25$ 

 $<0.01$ 

 $<0.01$  $<0.01$ 

 $20^{\mbox{th}}$  percentile or

Data are presented as mean ± standard deviation for continuous variables and n (%) for categorical variables. Low muscle strength was relative composite strength dichotomized as  $20^{th}$  percentile or

Data are presented as mean ± standard deviation for continuous variables and n (%) for categorical variables. Low muscle strength was relative composite strength dichotomized as

20th percentile according to the American College of Sports Medicine.

20<sup>th</sup> percentile according to the American College of Sports Medicine.

**Table 2**

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# **Table 3**

Association between Low Muscle Strength and Metabolic Syndrome Stratified by Age Association between Low Muscle Strength and Metabolic Syndrome Stratified by Age



Data are presented as odds ratio (OR) and 95% confidence interval (CI). Effect sizes are presented as Partial Eta Squared Data are presented as odds ratio (OR) and 95% confidence interval (CI). Effect sizes are presented as Partial Eta Squared.

upper and lower muscle strength. The reference group was the moderate-high muscle strength. Model 1: is adjusted for age, smoking status, and alcohol intake. Model 2: is adjusted for age, smoking status, Low muscle strength is defined as the lowest age-specific 20<sup>th</sup> percentile of relative upper or lower muscle strength, respectively. Low composite strength is defined as the lowest 20<sup>th</sup> percentile of relative upper and lower muscle strength. The reference group was the moderate-high muscle strength. **Model 1:** is adjusted for age, smoking status, and alcohol intake. **Model 2:** is adjusted for age, smoking status, Low muscle strength is defined as the lowest age-specific 20<sup>th</sup> percentile of relative upper or lower muscle strength, respectively. Low composite strength is defined as the lowest 20<sup>th</sup> percentile of relative alcohol intake, and BMI. Model 3: is adjusted for age, smoking status, alcohol intake, and cardiorespiratory fitness. alcohol intake, and BMI. **Model 3:** is adjusted for age, smoking status, alcohol intake, and cardiorespiratory fitness.

# **Table 4**

Threshold of Muscle Strength associated with Metabolic Syndrome Threshold of Muscle Strength associated with Metabolic Syndrome



Thresholds are presented as values of relative muscle strength (kg) divided by body weight (kg) with their respective sensitivity and specificity. The areas under the curve with the 95% confidence interval<br>are presented. M Thresholds are presented as values of relative muscle strength (kg) divided by body weight (kg) with their respective sensitivity and specificity. The areas under the curve with the 95% confidence interval are presented. **Model 1** is adjusted for age, smoking status, and alcohol intake. **Model 2** is adjusted for age, smoking status, alcohol intake, and BMI. **Model 3** is adjusted for age, smoking status, alcohol intake, and cardiorespiratory fitness.