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Effects of Muscular Strength on Cardiovascular Risk Factors and Prognosis

Enrique G. Artero, PhD[1,2], **Duck-chul Lee, PhD**[1], **Carl J. Lavie, MD**[3,4], **Vanesa España-Romero, PhD**[1], **Xuemei Sui, MD, MPH**[1], **Timothy S. Church, MD, MPH, PhD**[4], and **Steven N. Blair, PED**[1,5]

[1]Department of Exercise Science, Arnold School of Public Health, University of South Carolina. Columbia, South Carolina, USA

[2]Area of Physical Education and Sport, School of Education, University of Almería. Almería, Spain

[3]Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School - The University of Queensland School of Medicine. New Orleans, Louisiana, USA

[4]Preventive Medicine Laboratory, Pennington Biomedical Research Center. Baton Rouge, Louisiana, USA

[5]Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina. Columbia, South Carolina, USA

Abstract

Physical fitness is one of the strongest predictors of individual future health status. Together with cardiorespiratory fitness (CRF), muscular strength (MusS) has been increasingly recognized in the pathogenesis and prevention of chronic disease. We review the most recent literature on the effect of MusS in the development of cardiovascular disease (CVD), with special interest in elucidating its specific benefits beyond those from CRF and body composition. MusS has shown an independent protective effect on all-cause and cancer mortality in healthy middle-aged men, as well as in men with hypertension (HTN) and patients with heart failure. It has also been inversely associated with age-related weight and adiposity gains, risk of HTN, and prevalence and incidence of the metabolic syndrome. In children and adolescents, higher levels of muscular fitness have been inversely associated with insulin resistance, clustered cardiometabolic risk and inflammatory proteins. Generally, the influence of muscular fitness was weakened but remained protective after considering CRF. Also interestingly, higher levels of muscular fitness seems to some extent counteract the adverse cardiovascular profile of overweight and obese individuals. As many of the investigations have been conducted with non-Hispanic white men, it is important to examine how race/ethnicity and gender may affect these relationships. To conclude, most important effects of resistance training (RT) are also summarized, to better understand how higher levels of muscular fitness may result in a better cardiovascular prognosis and survival.

Key word or phrases

muscular strength; cardiorespiratory fitness; cardiovascular disease; resistance training

Physical fitness is one of the strongest predictors of individual future health status.[1] Health-related fitness has been characterized by the ability to perform daily activities with vigor, without undue fatigue, and by traits and capacities that are associated with a low risk for the development of chronic diseases and premature death.[2,3] Together with cardiorespiratory fitness (CRF), muscular or musculoskeletal fitness is also one of its main components, and

has been increasingly recognized in the pathogenesis and prevention of chronic disease.[4,5] In fact, muscle-strengthening activities are currently included in most of the institutional recommendations of exercise to maintain and improve overall health.[2,6-9]

Muscular fitness comprises the ability of a specific muscle or muscle group to generate force or torque (muscular strength, MusS), to resist repeated contractions over time or to maintain a contraction for a prolonged period of time (muscular endurance), and to carry out a maximal, dynamic contraction of a single muscle or muscle group in a short period of time (explosive strength, also called muscular power).[3] Among the components of muscular fitness, MusS has been traditionally the most frequently studied in relation to health. Thus, this term will be preferably used in the present manuscript unless otherwise indicated.

This report reviews the most recent literature on the effect of muscular fitness, especially MusS, in the development of cardiovascular disease (CVD), with special interest in elucidating its specific benefits beyond those provided by CRF, body composition and other related confounders.

Methods

The medical electronic databases MEDLINE, SCOPUS, and SPORTS DISCUS were used to search for studies relating muscular fitness (MusS, muscular endurance, and power) with CVD risk factors, incident CVD, and mortality. The search was preferably limited to articles from January 2000 to December 2011 and published in English, although additional studies were also identified from reference lists.

Findings

Muscular Strength and Mortality

Several prospective studies have shown that MusS is inversely associated with all-cause mortality.[10-23] Furthermore, some of these studies also explored the association with cause-specific mortality, including CVD.[11,17,20,21] However, all but one of these studies assessed MusS through a handgrip test,[22] which involves relatively small muscle groups. Only one of them included CRF as a critical confounder,[14] and most were short-term follow-ups (4-6 years)[10-12,16-19,23] or included only older adults (≥65 years),[10,12,16-20,22,23] which could be a problem with reverse causation in that muscle weakness could be due to poor health.

More recent epidemiological studies extend the association between MusS and mortality to younger populations. In the Aerobics Center Longitudinal Study (ACLS) cohort, we observed that a higher level of MusS, measured as 1 repetition maximum (1 RM) for bench and leg presses, was inversely and independently associated with deaths from all causes and cancer in 8762 men (mean age 42.3 years) followed on average 19 years.[24] The association was independent of central and total adiposity,[24,25] while the association with death from CVD was attenuated after adjustment for CRF (maximal treadmill time).[24] The attenuation in CVD mortality when including CRF may suggest a higher protection from this physical fitness component in the development of CVD, although we must also consider the difficulty of disentangling the combined effects of CRF and MusS in an observational study.[24] Future prospective studies should investigate whether MusS protects against CVD mortality beyond the benefits provided by CRF, especially among women, where studies are particularly scarce.

Hypertension (HTN) is clearly associated with an increased risk of CVD mortality.[26] Using the ACLS cohort, we explored the association between MusS (1 RM for bench and leg presses) and all-cause deaths among 1506 men with HTN (mean age 50.2 years) after 18

years of followup.[27] After comprehensive adjustment, including CRF, men with HTN and a high level of MusS had a lower risk of all-cause mortality. The lowest mortality risk was observed among participants with high levels of both MusS and CRF. However, the relatively small number of deaths, even during a nearly 20-year followup, did not allow examining disease-specific mortality risk.[27]

A study by Hulsmann et al[28] in patients with congestive heart failure (HF) provided insight into the association of MusS with CVD mortality. All participants (n=93; mean age 56±9 years) had a left ventricular (LV) ejection fraction <35%, and were followed for mortality on average 24 months. In this HF cohort, knee flexor muscles isokinetic strength significantly predicted mortality when expressed per kg of body weight, independent of CRF (peak VO2 during upright maximal bicycle test), neurohormones, and beta-blocker therapy.[28]

Muscular Strength and Incident CVD

To the best of our knowledge, we did not find in the literature any study investigating the association between MusS and the incidence of CVD while taking into account the confounding effects of CRF. However, the study by Silventoinen et al[29] must be highlighted given the sample size (1 145 467 men), participant age at baseline (18.2 years), the long followup (24.4 years) and the inclusion of different CVD endpoints [fatal and non-fatal coronary heart disease (CHD) and 3 types of stroke]. Elbow flexion, handgrip, and knee extension were used as indicators of MusS, and the analyses were adjusted for height, body mass index (BMI), systolic and diastolic blood pressure (BP), and social position. All MusS indicators were inversely associated with disease risk. For CHD and intracerebral infarction, handgrip strength was the best predictor, whereas for intracerebral and subarachoid hemorrhage, knee extension strength was the best predictor.[29] Whether this protective effect was due to MusS *per se* or rather, was expressing the role of general physical fitness status cannot be elucidated from this study.

Muscular Strength and CVD Risk Factors: Primary Prevention

Obesity—Two studies have hypothesized that MusS could have a role in preventing a positive energy balance and unhealthful weight gain. Mason et al[30] observed that a low level of muscular fitness was associated with higher odds of gaining at least 10 kg in 291 men and 315 women followed for 20 years. The assessment of muscular fitness included handgrip strength, push-ups, sit-ups, and sit-and-reach tests, and the association was independent of BMI, CRF (submaximal step test) and physical activity.[30] Using a considerably larger sample size (3258 men) although with shorter followup (8.3 years), we observed that MusS measured as 1 RM for bench and leg presses, was inversely associated with prevalence and incidence of excessive total and abdominal fat, defined as ≥25% and ≥102 cm, respectively.[31] The association remained after controlling for body weight, CRF, and other confounders.[31] These findings suggest that age-related weight and adiposity gains may be more pronounced among individuals with low levels of muscular fitness.

Hypertension—During a mean followup of 19 years, Maslow et al[32] analyzed the influence of MusS on incident HTN among 4147 men (mean age 43 years) in the ACLS cohort. In only prehypertensive men (systolic BP of 120-139 mm Hg or diastolic BP of 80-89 mm Hg), middle and high levels of MusS (ie, 1 RM) were associated with a reduced risk of HTN. Although it remained protective, the relationship was no longer significant after controlling for CRF. In normotensive men, such an association was not apparent.[32]

Metabolic syndrome—Skeletal muscle is the primary tissue for glucose and triglyceride (TG) metabolism, thereby providing rationale for its role in the metabolic syndrome (MetS).[5] Wijndaele et al[33] investigated the cross-sectional association of MusS and CRF

with a continuous MetS risk score in male and female Flemish adults aged 18-75 years. MusS was evaluated by measuring isometric knee extension and flexion peak torque, while CRF (peak VO2) was determined during a maximal cycle ergometer exercise test. The MetS risk score was based on waist circumference (WC), TGs, BP, fasting plasma glucose, and high-density lipoprotein (HDL) cholesterol. After adjusting for dietary intake, CRF, and other confounders, MetS risk was inversely associated with MusS in women. In men, however, adjustment for CRF attenuated this association. Independently of MusS however, CRF was inversely and more strongly associated with MetS risk in both men and women. The significant associations of MusS and CRF with the individual MetS risk factors were only partially mediated by central and total adiposity (WC and BMI, respectively).[33]

In the ACLS cohort, Jurca et al[34] reported an inverse association between MusS (ie, 1 RM) and prevalence of MetS in 8570 men aged 20-75 years. The association was notably attenuated when adjusted for CRF, whereas the effect of CRF was stronger and remained unchanged after adjusting for MusS.[34] Furthermore, MusS was inversely associated with MetS in low and moderate CRF groups, but did not provide any additional benefit in participants with high CRF. The joint protective effect of MusS and CRF on the prevalence of MetS was observed among overweight and obese men.[34]

The same authors analyzed the prospective association of MusS with MetS incidence in 3233 men after 7 years of followup.[35] After adjusting for potential confounders, such as number of risk factors at baseline, and family history of diabetes, HTN, and premature CHD, the authors observed an inverse association between 1 RM MusS and the risk of incident MetS. Further adjustment for CRF attenuated the association to being marginally not significant, although the risk of developing MetS was still significantly lower among men with high compared with low MusS.[35]

Dyslipidemia—A cross-sectional analysis in the ACLS cohort found no beneficial effects of greater MusS on total cholesterol, TGs, and low-density lipoprotein (LDL) and HDL cholesterol.[36] The study included 5460 men and 1193 women aged 20-69 years (mean age ~ 40 y), and took into account the possible confounding effect of CRF and body composition (sum of 7 skinfolds, BMI, or weight).[36]

Inflammatory factors—Inflammatory proteins have been negatively associated with MusS in the elderly.[37-39] The causal pathway leading from inflammation to loss of MusS has not been fully explained, but it has been suggested that low-grade inflammation may cause a decline of physical functioning through its catabolic effects on skeletal muscle.[40] No studies have been found relating MusS (as exposure) and inflammatory proteins (outcome) in middle-aged adults.

Muscular Strength and Cardiometabolic Health in Youth: Primordial Prevention

It is recognized that CVD is partly a pediatric problem because the onset of atherosclerosis seems to occur in early childhood.[41] Thus, timing is critical and interventions should not only focus on the modification of risk factors once they are established (primary prevention), but most importantly should prevent risk factor development in the first place (primordial prevention). Extensive evidence supports current physical activity recommendations for youth[42] for the inclusion of muscle-strengthening activities in addition to aerobic exercise to maintain cardiometabolic health at early ages and later in life.

Benson et al[43] investigated in 126 children (mean age 12.1±1.2 years) the cross-sectional association of CRF and MusS with estimated insulin resistance (Homeostasis Assessment Model2; HOMA2-IR). MusS was measured as 1RM for bench press and leg press, while CRF was determined as peak VO2 in a maximal treadmill walk protocol. Greater insulin

resistance was associated with greater WC, lower CRF, and lower MusS. Upper body MusS and WC were the only independent predictors of insulin resistance, accounting for 39% of the variance. Children in the highest and middle tertiles of upper body MusS were 98% less likely to have high insulin resistance than those with the lowest MusS, adjusted for maturation, WC, and BMI. When further adjusted for CRF, upper body MusS was slightly attenuated but still significant for the high MusS group and attenuated and of borderline significance for the moderate MusS group. Similar trends were present for high vs. low CRF, and this association was only slightly attenuated when adjusted for upper body MusS.[43]

In 460 boys and girls aged 13 to 18.5 years, we investigated the independent association of muscular fitness and CRF with a continuous cardiometabolic risk score based on TGs, LDL and HDL cholesterol, and glucose.[44] The 20m shuttle run test was used to assess CRF, and a muscular fitness index was created based on handgrip, standing long jump, and bent arm hang tests. After adjusting for age, maturation and CRF, muscular fitness presented an inverse association with cardiometabolic risk score in both genders, although statistically significant only among girls.[44] Similarly, those adolescents with higher CRF had a healthier cardiometabolic score after adjusting for age, maturation, and muscular fitness, with the association reaching statistical signification only in boys. Self-reported physical activity was not associated with the cardiometabolic cluster.[44] With 709 European adolescents (mean age 14.9±1.3 years) from 9 different countries, we observed that muscular fitness was negatively associated with clustered metabolic risk in both boys and girls, independent of CRF.[45] Handgrip strength and standing long jump were included in the muscular fitness score, whereas 20m shuttle run test was used to determine CRF. The continuous metabolic risk score included WC, systolic BP, TGs, total cholesterol/HDL cholesterol ratio, and insulin resistance (HOMA). Interestingly, the inverse association between muscular fitness and cardiometabolic risk persisted among non-overweight and overweight/obese adolescents.[45]

In this latter work with European adolescents,[45] muscular fitness presented a slightly stronger association with clustered cardiometabolic risk compared to CRF, which can be related to the use of 20m shuttle run test. In contrast, in a similar study by Steene-Johannessen et al,[46] the positive influence of CRF (peak VO2 in a cycle ergometry test) on clustered cardiometabolic risk was stronger than that provided by muscular fitness. Nevertheless, muscular fitness was inversely and independently associated with cardiometabolic risk after adjusting for CRF. The study comprised 1592 Norwegian youths aged 9 and 15 years, and muscular fitness included handgrip strength, standing long jump, sit-up and modified Biering-Sørensen test (endurance of trunk extensor muscles). Risk factors contained in the clustered cardiometabolic risk were systolic BP, TGs, HDL cholesterol, insulin resistance (HOMA), and WC.[46] Similar to our results,[45] the protective role of muscular fitness in Norwegian youths[46] was observed across both normal and overweight participants, being the association stronger in the overweight group.

A stronger association of CRF compared with MusS was also reported by Janz et al[47] in relation to several CVD risk factors, among 125 boys and girls aged 10.5 years at baseline. Authors investigated whether changes over 4 years in fat-free mass (bio-electric impedance), peak VO2 (cycle ergometry) and handgrip strength could predict levels of CVD risk factors in year five. After considering age, gender and fat-free mass, CRF explained 11% of the variability in total cholesterol/HDL cholesterol, 5% in LDL cholesterol, and 7% in both sum of 6 skinfolds and WC. MusS explained 4% of variability in systolic BP and 8% of variability in both skinfolds and WC.[47]

Apart from CVD traditional risk factors, muscular fitness has also shown to be inversely and independently associated with other emerging cardiometabolic biomarkers in youths. Ruiz et

al[48] investigated in 416 boys and girls (mean age 15.4±1.4 years) the association between muscular fitness (handgrip strength and standing long jump) and C-reactive protein, complement factors C3 and C4, ceruloplasmin, and prealbumin levels. After controlling for gender, age, maturation, weight, height, socioeconomic status, and CRF (20m shuttle run test), muscular fitness was inversely associated with C-reactive protein, C3, and ceruloplasmin. Moreover, C-reactive protein, which appears to be a predictor of CVD and is associated with CRF and especially with being overweight or obese,[49,50] was inversely associated with muscular fitness in overweight adolescents after controlling for body fat and fat-free mass.

Summarizing and Interpreting the Evidence

The observational studies reviewed suggest in middle-aged adults an independent protective effect of MusS on all-cause and cancer mortality,[24, 25] as well as all-cause mortality in men with HTN[27] and in patients with HF.[28] It has also been inversely and independently associated with age-related weight[30] and adiposity[31] gains, risk of HTN in prehypertensive men,[32] and prevalence and incidence of the MetS.[33-35] In children and adolescents, higher levels of muscular fitness have been inversely and independently associated with insulin resistance,[43] clustered cardiometabolic risk[44-47] and inflammatory proteins[48] (Table 1). In only a few studies, the protective influence of MusS became nonsignificant after considering CRF.[24,32,35,44] Also interestingly, higher levels of MusS seems to some extent counteract the adverse cardiovascular profile of overweight and obese individuals.[34,35,45,46,48]

Many studies (not discussed in this review) have focused on elderly people,[10,12,16-20,22,23] in whom frailty and sarcopenia make it difficult to explore the true connection between MusS and cardiovascular health. More prospective and intervention studies are needed in middle-aged adults in relation with incident CVD, being CRF and body composition crucial elements in this debate.

Valid and reliable MusS tests such as 1RM,[24,25,27,31,32,34-36,43] handgrip[30,44-48] or isokinetic tests,[28,33] do not require propulsion or lifting of the body mass. When using these tests, it is critical to somehow consider body size to express strength values. Different approaches have been used, such as normalizing strength per kg of body weight,[24,25,27,28,32,34,35,43,45,46] the use of allometric exponents,[33,47] the adjustment for body weight,[31,36,48] BMI,[24,25,27,30,36] total and/or central adiposity[25,36,43,48] or fat-free mass,[47,48] and also stratified analyses by BMI categories.[34,35,45,46,48] By doing this, we can more accurately compare individuals with different body sizes and focus on muscle quality rather than muscle quantity. The literature reviewed suggests that increasing or maintaining appropriate levels of MusS has many health-related implications other than those ascribed to morphological factors.

Potential mechanisms: insights from resistance training interventions

In different population studies, muscular fitness and CRF have shown to be moderately correlated.[24,30] Maintaining adequate MusS, muscular endurance, and flexibility will facilitate ability to carry out activities of daily living and to participate in physical activity, and this will likely help to maintain CRF. However, the reported level of that association is only moderate ($r \sim 0.3 – 0.4$),[24,25,27,30] indicating that muscular fitness may prevent CVD at least partially through biological pathways different than those associated with CRF.

Individual MusS level is influenced by several factors, such as age, gender, genotype, nutritional factors, or subclinical disease. Nevertheless, it is clear that muscle-strengthening activities are major determinants of MusS.[7,51] We have previously reported a strong and positive association between the frequency of self-reported resistance training (RT) and

maximal MusS in men enrolled in the ACLS,[34] which indicates that objective standardized MusS measurements can provide an adequate representation of RT exercise habits at the population level. It is likely that the protective role of MusS is a function of participation in regular muscle-strengthening activities, rather than a mere consequence of other factors affecting both MusS and cardiovascular health.

Several reviews have summarized the health-related benefits of RT.[7,52-57] Among those closely related with CVD, we must highlight the positive effects on muscle mass, muscle quality (increased strength for same muscle mass), and adipose tissue; maintenance of or an increase in resting metabolic rate; prevention of age-associated fat gains; reduction of visceral adipose tissue; improvements in blood glucose levels, basal insulin levels, insulin response, and insulin sensitivity; improvements in resting BP, and decreases in HbA1c in diabetic man and women[7,52-58] (Table 2). There is still little evidence that RT may improve lipoprotein-lipid profiles.[52] Other less explored mechanisms include improved endothelial function,[59] antioxidant defense,[60, 61] and immune function,[62] and decreased central arterial stiffness.[63]

Intensive RT characteristically increases LV wall thickness and mass, with little or no change in LV diameter,[7] a process that is termed concentric LV hypertrophy.[64,65] Concentric LV hypertrophy associated with RT appears to be a response to the pressure load (in contrast to the volume load of aerobic exercise) and serves to reduce the systolic burden per myofiber, thereby preserving normal LV wall stress. The increase in skeletal muscle strength induced by RT results in a lower hemodynamic stress (heart rate and systolic BP) for a given skeletal muscle force after RT.[7] Also, although RT does not impose a large aerobic burden, some studies have demonstrated a modest increase in peak VO2 and decreases in submaximal heart rate and systolic BP during aerobic exercise after a program of RT.[7]

Among the many studies of RT in healthy adults, there have been no reported cardiovascular complications. The American College of Sports Medicine[66] and the American Heart Association[7] indicate that the contraindications to RT are similar to those for aerobic exercise. Thus, the same screening criteria used for healthy adults before participation in aerobic exercise would apply.[52]

Conclusions and Future Directions

Considerable evidence supports the important and independent role of MusS in the prevention of CVD. However, as most efforts have focused on mortality and CVD risk factors, more prospective and intervention studies are needed in relation with incident CVD. Whenever possible, CRF, body composition and other related factors should be considered. Also, the majority of investigations have been conducted with non-Hispanic white men,[24,25,27,31,32,34,35] so it is important to examine how race/ethnicity and gender may affect these relationships.[67] Special attention should be paid to growth and development stages,[68] when CRF, MuSs and body composition are mostly determined.

To conclude, RT must be considered in addition to aerobic exercise in the prevention and treatment of CVD, since both MusS and CRF may provide unique benefits. In fact, RT might be a more attractive type of exercise for overweight and obese individuals, who are at a higher risk of developing CVD and who may be averse to aerobic exercise. Clinicians and fitness professionals are directed to several guidelines and statements that have been developed for the prescription of RT in different populations: apparently healthy middle-aged and older adults,[53] children and adolescents,[69,70] and patients with CVD.[7]

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Table 1

Mechanisms by which muscular strength may improve prognosis of CVD.

Higher muscular strength levels seem to be associated with:
Lower total and abdominal adiposity
Lower weight and adiposity gain
Healthier levels of MetS components (BP, WC, TGs, glucose, HDL cholesterol) and lower incidence of MetS
Lower risk of developing HTN (some evidence in prehypertensive individuals)
Lower insulin resistance, HOMA (evidence in adolescents)
Lower chronic inflammation (evidence in children, adolescents and elderly people)

Abbreviations: BP, blood pressure; CVD, cardiovascular disease; HDL, high-density lipoprotein; HOMA, homeostasis model assessment; HTN, hypertension; MetS, metabolic syndrome; TGs, triglycerides; WC, waist circumference.

Table 2

Comparison of effects of aerobic exercise with resistance exercise on health and fitness variables.

Variable	Aerobic Exercise	Resistance Exercise
Total body fat	↓↓	↓
Intra-abdominal fat	↓↓	↓↔
Lean body mass	↔	↑↑
Body weight	↓	↔
Resting metabolic rate	↑	↑↑
Muscular strength	↔	↑↑↑
Muscular mass	↔	↑↑
Muscular power	↔	↑
Capillary density	↑	↔
Mitochondrial volume	↑↑	↓↔
Mitochondrial density	↑↑	↓↔
Basal insulin levels	↓	↓
Insulin sensitivity	↑↑	↑↑
Insulin response to glucose challenge	↓↓	↓↓
Resting heart rate	↓↓	↔
SBP at rest	↓↓	↓
DBP at rest	↓↓	↓
Peak VO2	↑↑↑	↑ ↔
Submaximal and maximal endurance time	↑↑↑	↑↑
Submaximal exercise rate-pressure product	↓↓↓	↓↓

↑ Indicates increased; ↓, decreased; ↔, negligible effect; 1 arrow, small effect; 2 arrows, moderate effect; 3 arrows, large effect.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.