Cardiorespiratory Fitness and Muscular Strength on Arterial Stiffness in Older Adults

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ABSTRACT
ALBIN, E. E., A. G. BRELLENTHIN, J. A. LANG, J. D. MEYER, and D.-C. LEE. Cardiorespiratory Fitness and Muscular Strength on Arterial Stiffness in Older Adults. Med. Sci. Sports Exerc., Vol. 52, No. 8, pp. 1737–1744, 2020. Purpose: To evaluate the independent and combined associations of cardiorespiratory fitness (CRF) and muscular strength (MS) with arterial stiffness (AS), a strong predictor of cardiovascular disease, in older adults. Methods: This cross-sectional study included 405 older adults (mean age, 72 yr). Cardiorespiratory fitness was assessed by time (s) to complete a 400-m walking test and MS by maximal handgrip strength (kg). Carotid-femoral pulse wave velocity was used to assess AS. High AS was defined as a pulse wave velocity of ≥10 m·s⁻¹, a previously established threshold for increased cardiovascular risk. Poisson regression was used to calculate prevalence ratios (PR) and 95% confidence intervals (CI) of having high AS across sex-specific tertiles of CRF and MS. Muscular strength and CRF were further dichotomized into either “weak” or “unfit” (lower one third for each), or “strong” or “fit” (upper two thirds for each) to investigate the combined associations of CRF and MS with high AS. All analyses were adjusted for potential confounders, including MS for CRF and CRF for MS. Results: Sixty-nine (17%) participants had high AS. Compared with lower CRF, PR (95% CI) of having high AS were 0.53 (0.38–0.95) and 0.69 (0.38–1.23) for middle and upper CRF, respectively. Compared with lower MS, PR (95% CI) of having high AS were 0.81 (0.49–1.34) and 0.52 (0.29–0.92) for middle and upper MS, respectively. In the joint analysis, compared with the “unfit and weak” group, PR (95% CI) of having high AS were 0.72 (0.38–1.35), 0.58 (0.29–1.16), and 0.46 (0.25–0.85) for “unfit and strong,” “fit and weak,” and “fit and strong” groups, respectively. Conclusions: Higher levels of CRF and MS were independently associated with lower (healthier) levels of AS in older adults. Key Words: PULSE WAVE VELOCITY, 400-M WALK, HANDGRIP STRENGTH, PHYSICAL ACTIVITY

Arterial stiffness (AS) is the decreased compliance of the large central arteries and represents structural and cellular changes to these arteries, which are thought to result from aging and many disease states (obesity, diabetes, insulin resistance, dyslipidemia, and hypertension) (1,2). Arterial stiffness is an emerging strong and independent predictor of cardiovascular disease (CVD) (1,3). For example, Vlachopoulos et al (3) found that individuals with high AS had twice the risk of CVD events and CVD mortality (relative risk [RR], 2.26; 95% confidence interval [CI], 1.89–2.70 and RR, 2.02; 95% CI, 1.68–2.42, respectively) compared with individuals with low AS. Specifically in a population of older adults, Mitchell et al (4) found that for every standard deviation increase in AS, there was a 1.48 times increased risk of having a major CVD event. Age is the strongest determinant of AS (1,5), with age-related increases in AS observed in healthy populations (5,6). Arterial stiffness also strengthens CVD risk prediction when added to traditional risk factors, such as blood pressure, and may provide unique predictive insight that is undetected by traditional risk factors. This is demonstrated in a meta-analysis reporting that even in individuals with normal blood pressure (no hypertension), people with high AS had a significantly greater risk of CVD events (RR, 1.28; 95% CI, 1.15–1.42) (7).

Higher levels of physical activity are associated with lower AS in older adults (8,9). Regular aerobic and resistance exercise participation, often reflected by higher cardiorespiratory fitness (CRF) and muscular strength (MS), may attenuate AS (2,10–13). Both aerobic and resistance exercise have been shown to improve traditional CVD risk factors and many other conditions that advance vascular aging related to AS (2,10). Higher levels of CRF, which is often used to represent recent aerobic exercise participation, are consistently associated with reduced AS in populations generally predisposed to high AS including older adults (5,6,14–16). In contrast, very few studies have examined the association between MS and AS in any population (15,17–19). The majority of the current MS and AS studies have been conducted in young adults (and primarily men), and the few studies in older adults provide mixed
RESULTS (15,19). Additionally, even though there is a well-known relationship between CRF and AS, only one of these studies adjusted for CRF in their analysis of MS. Muscular strength is associated with beneficial CVD health outcomes independent of CRF, but there are limited data on the relationship between MS and AS (17,18). It is important to account for MS when examining the relationship of CRF with AS, and vice versa, to determine the independent associations (13). Examining the joint associations between CRF and MS with AS could provide novel information and reveal the relative importance of CRF or MS and the potential additive benefits of both. This information would influence how and what type of physical activity and exercise (aerobic or resistance) could be recommended to reduce arterial stiffening, due to age, CVD, or other chronic diseases.

The purpose of this study was to investigate the independent and combined associations of objectively-measured CRF and MS with AS in older adults using data from a prospective cohort, the Physical Activity and Aging Study (PAAS). It was hypothesized that: 1) higher CRF would be associated with lower AS, independent of MS; 2) higher MS would be associated with lower AS, independent of CRF; and 3) the combined association of CRF and MS with AS would be stronger than either CRF or MS alone.

METHODS

Study Participants

The PAAS is an ongoing prospective observational cohort study of older adults at least 65 yr. Since the addition of AS assessment in 2017, 497 men and women participated in PAAS. We excluded 52 individuals with diabetes and 32 individuals reporting CVD (myocardial infarction, stroke, or congestive heart failure) to minimize strong potential confounding effects on AS. Additionally, eight individuals with missing data for CRF (400-m walk time), MS (handgrip strength), AS (pulse wave velocity [PWV]), or any covariates were excluded from this analysis. Therefore, 405 older adults (mean ± SD age, 72 ± 6 yr) were included in this study. Procedures adhered to the Declaration of Helsinki and were approved by the local institutional review board. All participants provided written informed consent before participation.

Data Collection Procedures

Assessments occurred over two visits separated by 1 wk. At the first visit, participants completed a medical history questionnaire, as well as fitness, function, and strength assessments. A week later, participants completed fasted assessments (no food, alcohol, or caffeine 12 h before assessments), including blood pressure, AS, and a blood draw. Between visits, participants were given pedometers to record their daily steps.

Cardiorespiratory fitness. In older adults, the 400-m walking test is considered an appropriate and valid method to estimate CRF. Completion times from the 400-m walking test are associated with \( VO_{2\text{max}} \) from maximal treadmill test \( (r = -0.79) \), submaximal treadmill test \( (r = -0.66) \), and estimation with prediction equation \( (r = -0.60) \) (20,21). The 400-m walking test demonstrates excellent reproducibility when tests were repeated a week apart (intraclass correlation coefficient [ICC], 0.95; 95% CI, 0.92–0.97) (20).

Cardiorespiratory fitness was assessed by the time (s) required to walk 10 laps as fast as possible on a 20-m-long course (total, 400 m). Cones marked the ends of the course, and participants were instructed to walk as quickly as possible, without running (21,22). Participants were allowed to rest up to 60 s if they remained standing. The maximum time allowed was 15 min, and all participants included in this study finished the test within 15 min.

Muscular strength. Handgrip strength is associated with overall MS in older adults \( (r = 0.26–0.52) \) (23). Muscular strength was assessed by handgrip strength, using a digital dynamometer (Jamar Plus+12–064; Lafayette Instrument, Lafayette, IN). The dynamometer was correlated with known weights \( (r = 0.99) \) and demonstrated both within-instrument \( (r = 0.82) \) and interinstrument (ICC range, 0.90–0.97) reliabilities (24,25). The dynamometer was adjusted individually so that the middle two fingers formed a 90° angle when gripping the device. During the assessment, participants sat with their wrist in a neutral position and elbow at a 90° angle. They were instructed to maximally grip the dynamometer, holding the maximum contraction for 2 s. Three trials were completed on each hand with 1 min of rest between each measurement. Overall handgrip strength was calculated by first taking the maximum contraction of the three trials from each hand and then averaging together the left- and right-hand maximums (11).

Arterial stiffness. Carotid-femoral PWV is the gold standard and most frequently used index for assessing AS (26,27). Carotid-femoral PWV was measured using the Sphygmocor XCEL (AtCor Medical, Itasca, IL) device, following previously published guidelines (27–29). The PWV measured by the Sphygmocor XCEL device has been shown to be both accurate (rated “excellent,” mean difference < 0.05 m s\(^{-1}\)) and valid according to the ARTERY Society guidelines (30). Additionally, XCEL PWV measurements demonstrated repeatability within sessions on the same day (ICC, 0.99) and between sessions on different days (ICC, 0.98) (31).

The PWV assessment was performed while the participants were overnight fasted (no food, alcohol, or caffeine for 12 h overnight before assessment), in the same room (centrally controlled temperature) during the same morning timeframe for all participants, and after 10 min of supine quiet rest (28,29). Participants were in a supine position with a femoral pressure cuff placed on their upper left thigh. The Sphygmocor XCEL device uses vascular path length divided by transit time to estimate PWV. To measure the vascular path length (distance), linear measurements from the supraprosternal notch to both the site of carotid applanation tonometry and the top of the femoral cuff were obtained. These measurements were taken using a tape measure and caliper for carotid and femoral sites, respectively. The vascular path length was estimated using the
“subtraction method” (suprasternal notch-femoral cuff site minus suprasternal notch-carotid tonometer site) (28–30). To estimate the transit time of pressure waveforms, the femoral cuff obtained a volumetric displacement waveform while application tonometry simultaneously acquired the carotid pulse (30). At least two PWV measurements were performed, and if the first two differed by more than 0.5 m·s⁻¹, a third measurement was taken. Median PWV value was used following the guidelines (27,29). For the Poisson regression, high AS was defined as a PWV of ≥10 m·s⁻¹, as it has been established as a threshold for increased cardiovascular risk (27,29).

**Covariates.** Height, weight, mean arterial pressure (MAP), and the blood lipid panel were also completed while overnight fasted. Height (cm) was measured with a standard stadiometer and weight (kg) using a digital scale. Body mass index (BMI) was calculated using the weight (kg) divided by height (m) squared. Mean arterial pressure was assessed using the Sphygmocor XCEL automated device (AtCor Medical, Itasca, IL). The participant was supine with a brachial cuff placed on the left arm. The device automatically took three readings. Mean arterial pressure from the Sphygmocor XCEL device is used because analysis of PWV measurements should take into account MAP at the time of the PWV measurement (28,29). A phlebotomist drew 5 mL of blood from a superficial arm vein, and blood chemistry analysis provided a lipid profile (total cholesterol, low- and high-density lipoprotein cholesterol, and triglycerides) and blood glucose. Medical history and/or current medications (hypertension, hypercholesterolemia, or nonsteroidal anti-inflammatory [NSAID] medications) and blood pressure medication (yes or no), and hypercholesterolemia (yes or no). All analyses were conducted using SAS software version 9.4 (SAS Institute, Inc., Cary, NC) and two-sided P values <0.05 were considered significant.

**RESULTS**

**Participant characteristics.** Sixty-nine (17%) older adults were identified as having high AS. Characteristics of the study sample by thirds of CRF and MS are reported in Table 1. Participants in the upper CRF group were more likely to be younger, stronger, more physically active (steps per day), with lower BMI, systolic blood pressure, MAP, blood pressure medication usage, and PWV. Participants in the upper MS group were also more likely to be younger and fitter, with lower systolic blood pressure and PWV.

Compared with lower CRF, the PR (95% CI) for having high AS in the middle and upper CRF categories were 0.46 (0.26–0.81) and 0.54 (0.31–0.96), respectively, after adjusting for age and sex. Additionally, a linear trend was observed in this model (model 1, P for trend = 0.028) (Table 2). After further adjustment for MAP, BMI, lifestyle factors, and blood pressure or NSAID medications, PR (95% CI) of high AS among the middle CRF was 0.51 (0.29–0.91), and the reduced odds in upper CRF was no longer significant (PR, 0.65; 95% CI, 0.37–1.17). The reduced odds in middle CRF remained significant after further adjustment for MS (PR, 0.53; 95% CI, 0.30–0.95) (Table 2).

The upper MS tertile had significantly reduced odds of high AS in all three models, whereas the middle tertile did not have reduced odds of high AS in any of the models. Compared with lower MS, PR (95% CI) for upper MS was 0.50 (0.28–0.92), after adjustment for age and sex, and 0.52 (0.30–0.92) after further adjustment for BMI, MAP, lifestyle factors, and blood pressure and NSAID medications (Table 2). This association remained statistically significant after further adjustment for CRF (0.52 [0.29–0.92]). Additionally, there were significant linear trends across MS tertiles in all three models (Table 2).
Additional analyses, stratified by sex, physical activity, BMI, hypertension, blood pressure medication, and hypercholesterolemia, that are considered as other possible risk factors of AS were conducted. Overall, the stratified analysis revealed consistent similar associations across all strata and confirmed no interactions for other possible risk factors (all interaction P > 0.05).

A joint analysis was conducted to investigate the combined associations of CRF and MS with high AS. The means (standard deviations) of PWV (m·s⁻¹) were 9.4 (1.8), 9.0 (1.6), 8.2 (1.6), and 8.3 (1.8) for the “unfit and weak,” “unfit and strong,” “fit and weak,” and “fit and strong” groups, respectively. The interaction P value between the dichotomized variables of CRF (fit and unfit) and MS (weak and strong) on AS was P = 0.796. Compared with the “unfit and weak” group, the “unfit and strong,” “fit and weak,” and “fit and strong” groups had PR (95% CI) of 0.72 (0.38–1.35), 0.58 (0.29–1.16), and 0.46 (0.25–0.85), respectively (Fig. 1). When using the “fit and strong” group as the reference, PR (95% CI) of having high AS were 1.24 (0.65–2.39) (P = 0.51) and 1.54 (0.81–2.91) (P = 0.18) for “fit and weak” and “unfit and strong” groups, respectively (not depicted). When directly comparing the “unfit and strong” group with the “fit and weak” group, there was no significant difference between the groups in the PR of high AS (P = 0.55).

DISCUSSION

The major finding of this study is that both CRF and MS are independently associated with reduced odds of having high AS in older adults. Additionally, a joint analysis revealed that
the relative contribution of CRF and MS appears to be similar when directly comparing the “fit and weak” group with the “unfit and strong” (P = 0.55). Overall, the “fit and strong” group showed the lowest PR of having high AS (although it was not significantly different from the “unfit and strong” or “fit and weak” groups) in this older adult sample, suggesting a possible additive benefit of being both fit and strong on AS. However, further prospective study is clearly required to confirm this finding.

Cardiorespiratory fitness is consistently inversely associated with AS in cross-sectional studies of various populations, including older adults (5,15,16). Our results are consistent with this previously established relationship. Additionally, the results from Poisson regression suggest that the association between higher CRF and reduced PR of having high AS is independent of MS (Table 2, model 3). However, the association is not as strong as expected (e.g., upper CRF was not significantly associated with high AS in models 2 and 3), which is confirmed by a weak correlation (r = 0.19, P < 0.001) between CRF and AS in our cohort of relatively healthy older adults. However, Jae et al. (14) reported an inverse association of similar magnitude between CRF and AS (measured with PWV) in middle-age men with and without metabolic syndrome. Additionally, a significant moderate correlation between $\bar{V}O_{2\text{max}}$ and large artery elasticity has been reported in older women (15). In contrast, an investigation by Vaitkevicius et al. (5) found that the association between CRF and AS tends to strengthen with age as they reported a strong association between higher CRF and lower AS in older adults compared with young or middle-age adults. Therefore, the inverse association between CRF and AS in our cohort was expected but slightly weaker compared with other studies possibly due to different study design, statistical analysis, or assessment methods of CRF and AS.

The slightly weaker association between CRF and AS in our sample could potentially be due to more robust data analysis including comprehensive potential confounders (e.g., MAP, BMI) in the regression, which attenuates the association between CRF and AS. For example, the addition of MAP to the model may be one reason why the upper CRF group went from significant to nonsignificant between models 1 and 2 (Table 2). An exploratory linear regression analysis indicated that among all the predictors, MAP explained the largest portion of the variance between CRF and PWV (data not depicted). Because the lower and middle CRF groups had similar MAP values while the upper CRF group had relatively lower MAP, the association of CRF with high AS may be more apparent between the lower and middle CRF groups because they are less confounded by MAP. Furthermore, lower BMI in the upper CRF group may also include older adults with unintentional weight loss, a preclinical symptom of chronic disease, which might also affect AS (3). Other possible explanations may include different assessments of CRF.

**FIGURE 1**—PR of high AS by combined categories of CRF and MS. The model was adjusted for age, sex, mean arterial pressure, BMI, physical activity (insufficiently active or active), current smoking status (yes or no), heavy alcohol intake (yes or no), blood pressure medication (yes or no), and nonsteroidal anti-inflammatory medication (yes or no). High AS is a PWV $\geq 10$ m·s$^{-1}$. CRF is the time (s) to complete 400-m walking test. Muscular strength is overall handgrip strength (kg). Participants were divided into four groups based on CRF and MS, where “unfit” and “weak” were the lower third of CRF and MS, respectively, and “fit” and “strong” were the upper two thirds of CRF and MS, respectively. The number of individuals (cases of higher AS) in the “unfit and weak,” “unfit and strong,” “fit and weak,” and “fit and strong” groups were 72 (25), 62 (13), 62 (9) and, 209 (22), respectively.
(e.g., 400-m walking test in this study vs treadmill or bike test in other studies) or different samples (e.g., our older adult participants are relatively healthier and fitter since participants volunteered to join this open cohort study). The lower, middle, and upper CRF tertiles’ walking paces during the 400-m walking test were equivalent to 3.5, 4.3, and 5.0 METs, respectively, indicating the relatively high physical fitness and functional ability of this older adult sample (34).

There is limited research on the relationship between MS and AS. An inverse relationship between MS and AS has been shown in young adults from cross-sectional studies (17,18), and mixed results have been shown in older adults (15,19). Our results demonstrate a significant inverse relationship between MS and AS. In those studies that found similar associations, there were weak correlations \( r = -0.11 \) to \(-0.23 \) between MS and AS (17–19) and moderate correlations \( r = 0.32 \) between MS and large artery elasticity (15). However, Fahs et al. (17) reported strong associations between higher MS and lower odds of AS (0.14 [0.02–0.92]), independent of CRF, despite using a lower PWV cut-point of 6.6 m·s\(^{-1}\) for defining high AS. Our results follow a similar pattern indicating significantly reduced PR of high AS with higher levels of MS (Table 2) though there was a relatively weak, significant correlation between MS and PWV \( r = -0.11, P = 0.03 \). Fahs et al. (19) also found that MS was more strongly related to AS than lean body mass, suggesting that muscle function is strongly related to AS. Although hand-grip strength has been shown to be representative of overall MS, it is also a good measure of muscular function in older adults (35). In an exploratory analysis, we further refined MS by using tertiles of relative handgrip strength (maximum grip strength/body weight) rather than absolute hand grip strength. The PR (95% CI) for the middle and upper relative MS tertiles in the fully adjusted model were 0.46 (0.26–0.81) and 0.59 (0.33–1.05), respectively, indicating slightly stronger associations of relative strength with AS in older adults, as well as highlighting the potential confounding effect of body weight on the associations between MS and AS.

Muscular strength rather than CRF appeared to be more consistently associated with reduced AS. One potential explanation is the relatively high CRF in this sample. For example, the Health, Aging and Body Composition Study (Health ABC) included 3075 older adults who performed the 400-m walking test, and most of our sample falls within their fastest two quartiles (201–323 s). Furthermore, the middle and upper CRF tertiles’ walking times were faster than the Health ABC cohort’s average (320 s), for both women and men (Table 1) (22,36). This indicates that our sample may have higher than average CRF and could potentially be exhibiting a ceiling effect; that is, the association between CRF and MS may have been stronger if there was a wider range of 400-m walking times with more unfit participants. In contrast, the distribution of MS scores in our cohort was consistent with the distributions of other large studies that also used handgrip strength (37,38). MS was also more strongly associated with other indicators of AS. For example, pulse pressure is sometimes considered as a surrogate marker of AS in large arteries. While there are no established cut points for high pulse pressure as a risk factor for CVD, a previous study has found that a pulse pressure of 50 mm Hg or higher is related to an increased risk of acute cardiovascular events (39). The results for the associations of MS tertiles with high pulse pressure were similar with the upper MS group showing significantly reduced PR of high pulse pressure compared with the lower MS group in all three models. Interestingly, there were no significant findings between CRF and high pulse pressure, indicating that MS may have greater implications for AS in larger blood vessels.

Even though they often are correlated with one another \( r = -0.32, P < 0.001 \) in this sample), CRF and MS are generally improved by different types of exercise (aerobic exercise for CRF and resistance exercise for MS). Both aerobic and resistance exercises are associated with improvements in functional components of arteries (i.e., endothelial function, inflammation, and sympathetic activity) that contribute to reductions in AS (12). Additionally, although not as thoroughly studied as aerobic exercise, resistance exercise may provide unique hormonal and metabolic benefits, such as improved insulin response and increased basal metabolic rate, that may influence AS (2,13). Therefore, investigating the relative importance between CRF and MS on AS in this study is useful to provide information to help answer the question “What type or combination of exercise is more effective to prevent CVD?” that is important to develop more comprehensive physical activity guidelines. In the joint analysis, the “fit and strong” group had the lowest PR of having high AS compared with the “unfit and weak” reference group. However, the comparable PR in “unfit and strong” and “fit and weak” groups, and the fact that they were not significantly different from the “fit and strong” group, may also suggest that the relative contributions of CRF and MS are similar. However, these results should be interpreted cautiously due to the low case numbers in some groups.

A limitation of this study is the lack of diversity in this cohort of older adults, which is largely white, highly educated, and living independently, thus the results may be different in other older adult populations. There are other factors, such as eating, hydration status, and room temperature, that can influence the assessment of PWV. We minimized these confounding effects by having participants overnight fast before assessment, encouraging them to continue drinking water through the fast, and completing measurements at the same time of day for all participants. Also, room temperature was centrally controlled at a similar level throughout the study. Other limitations include insufficient information on dietary patterns or vitamin or supplement usage as well as not adjusting for demographic variables such as race/ethnicity or socioeconomic status due to the homogeneity of the sample. Lastly, since this is a cross-sectional analysis, we cannot determine causation or direction of the associations. Higher CRF and MS may lower AS just as higher AS may lower CRF or MS, or there may be other unaccounted variables that underlie the relationships. However, this study provides rationale and need
for further prospective analysis of CRF and MS with AS, which is a strong, emerging, and independent predictor of CVD, especially in older adults since aging is one of the main contributors of increased AS.

In conclusion, higher levels of both CRF and MS were associated with a lower prevalence of high AS in our older adult sample. However, the results from this cross-sectional study warrant further research (prospective studies and randomized control studies) on the potential benefits of different types and combinations of exercise and fitness on AS in older adults.

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