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Role of Muscular Strength on the Risk of Sudden Cardiac Death in Men

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To the Editor: The role of cardiorespiratory fitness (CRF) on sudden cardiac death (SCD) has been summarized (1), with the risk of SCD decreasing by 14%-22% per 1-MET increase in CRF (1). Recently, the Mayo Clinic Proceedings has not only emphasized CRF (2–4), but also papers on resistance exercise (RE) and muscular strength (MusS) (5–7). However, there is no study about the role of muscular strength (MusS) on SCD, even though MusS was inversely and independently associated with all-cause mortality in healthy men (8). Consequently, this report investigated the role of MusS as a predictor of SCD independent of potential risk factors and explored the combined influence of MusS and CRF on the risk of SCD.

This report is based on data from the Aerobics Center Longitudinal Study (ACLS), a prospective observational investigation. For the present analysis, men 18 years or older with data on MusS and potential confounders (e.g., medical history, lifestyle behaviors) as well as at least one year of mortality follow-up were included. Participants were predominantly white, well-educated, and belonged to the middle and upper socioeconomic strata. We could not include women due to the very limited SCD cases (n=2).

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MusS was assessed in the upper and lower body using a standardized bench and leg press strength testing protocol as previously reported (8). A composite strength score was computed by averaging together the body weight-adjusted then standardized values of bench and leg press. For SCD events, the National Death Index was the primary data source for mortality surveillance, augmented with death certificates (1). Cox proportional hazard regression was used to compute hazard ratios (HRs;95% confidence intervals, CIs) of SCD for thirds of MusS (Models 1-3 in Table 1).

A total of 8,116 men were included, and 23 cases of SCD occurred over an average follow-up of 18.4 (2.8) years. Compared with the lower third of MusS, there was 69% reduced risk of SCD in the middle of MusS after adjusting for Model 3 (Table 1). Although statistically not significant, we also observed about 50% reduced risk of mortality in the upper third of MusS in all models. In additional analyses, we further adjusted for CRF in a subsample of men with complete and valid CRF data (n=7,669; 21 SCD cases) and found that there was a 58% reduced risk of SCD in the middle third of MusS, although no longer statistically significant (0.42[0.13-1.36]). Moreover, a 1-standard deviation increase in MusS was associated with 43% reduced risk of SCD in Model 1.

In the subsample with CRF data, men were dichotomized into weak (lower third MusS) or strong (middle and upper thirds MusS) and unfit (lower third CRF) or fit (middle and upper thirds CRF) for a joint analysis as previously done (8). Compared with the weak and unfit group as a reference, the HRs (95% CI) for the unfit and strong, fit and weak, and fit and strong groups were 0.39 (0.10-1.50), 0.61 (0.17-2.26), and 0.28 (0.08-0.94), respectively, after adjusting for the full set of confounders in Model 3, indicating a potential additive benefit of being fit combined with being strong.

MusS was associated with a reduced risk of SCD, independent of several risk factors, including aerobic physical activity. However, the results were attenuated and no longer significant when CRF was included in the model. It is not clear whether this is due to the confounding effects of CRF on the association or due to the reduced sample size and SCD cases. However, we noted that there was a 58% reduced risk of SCD in the middle third of MusS even after adjusting for CRF, although not significant. Moreover, the joint analysis indicated that being both fit and strong may provide the greatest benefit on preventing the risk of SCD significantly by 72%. To our knowledge, this is the first study to report the protective role of MusS on SCD risk independent of several risk factors, and the first to report the additional value of the combination of high MusS and CRF for the reduction of SCD risk.

These findings offer new insights into the prevention of SCD through increasing MusS in addition to the previously documented protective benefits of CRF (1). Moreover, this also supports previous research indicating that both MusS and CRF predict all-cause mortality risk (8).

The apparent protective effect of MusS against the risk of SCD might be due to the direct effect of muscle strength, which is considered an index of muscle quality and function that is generally improved by RE. RE associated with better functional capacity, metabolic and

inflammation profiles (9), and recently, with better survival (10). In fact, results from intervention studies indicate that resistance training enhances MusS and endurance, muscle mass, functional capacity, risk profile for CVD, and quality of life (9), which are well known predictors of overall mortality.

This study is limited by the small sample size and SCD cases, which may partially contribute to no significant result in the upper third of MusS. However, the risk-reduction of SCD for those with moderate MusS or the combination of both high MusS and CRF was even stronger (69% or 72%, respectively) than previously found for CRF alone (44%-48% risk-reduction) in a larger sample of the ACLS cohort (n=59,611) (1). Further studies are needed to assess the combined effects of MusS and CRF in the prevention of SCD.

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TABLE 1.

Sample Characteristics and Association of Muscular Strength (MusS) with Risk of Sudden Cardiac Death

	Tertiles of Muscular Strength				P-value
	Overall	Lower	Middle	Upper	
N	8,116	2,696	2,723	2,697	
Age, mean (SD), years	42.0 (9.7)	42.5 (9.6)	42.1 (9.7)	41.4 (9.8)	<0.0001
Body Mass Index, mean (SD), kg/m ²	26.1 (3.7)	27.3 (4.4)	25.8 (3.2)	25.2 (2.9)	<0.0001
Meeting Aerobic Guidelines, No. (%) [*]	3056 (38)	840 (31)	992 (36)	1224 (45)	<0.0001
Current Smoking, No. (%) [†]	1315 (16)	493 (18)	464 (17)	358 (13)	<0.0001
Heavy Alcohol Drinking, No. (%) [‡]	1991 (25)	695 (26)	705 (26)	591 (22)	0.0006
Parental CVD, No. (%) [§]	2359 (29)	804 (30)	802 (29)	753 (28)	0.2641
Abnormal ECG, No. (%)	459 (6)	170 (6)	153 (6)	136 (5)	0.1326
Hypertension, No. (%) [#]	2177 (27)	848 (31)	685 (26)	644 (24)	<0.0001
Diabetes, No. (%) ^{**}	226 (3)	106 (4)	64 (2)	56 (2)	<0.0001
CRF, mean (SD), METs ^{††}	12.4 (2.5)	11.3 (2.3)	12.4 (2.4)	13.4 (2.5)	<0.0001
Upper Body Strength:					
kg	72.0 (17.7)	62.0 (12.7)	70.3 (12.9)	83.7 (19.3)	<0.0001
kg/kg of body weight	0.9 (0.2)	0.7 (0.1)	0.9 (0.1)	1.1 (0.2)	<0.0001
Lower Body Strength:					
kg	138.1(27.6)	126.2(26.1)	136.8(23.7)	151.2(26.8)	<0.0001
kg/kg of body weight	1.7 (0.3)	1.4 (0.2)	1.7 (0.2)	1.9 (0.3)	<0.0001
Composite Strength Score	8.6x10 ⁻⁶ (0.91)	-0.81 (0.48)	-0.05 (0.44)	0.87 (0.79)	<0.0001
MusS and Risk of SCD					
		Tertiles of Muscular Strength			Per 1-SD increase ^{##}
		Lower	Middle	Upper	
No. of Participants		2696	2723	2697	8116
No. of SCD		13	4	6	23
Hazard Ratio (95% CI) Model 1 ^{‡‡}		1.00 [ref]	0.28 (0.09- 0.87)	0.43 (0.16-1.14)	0.57 (0.33-0.96)
Hazard Ratio (95% CI) Model 2 ^{§§}		1.00 [ref]	0.31 (0.10-0.97)	0.48 (0.17-1.32)	0.61 (0.35-1.05)
Hazard Ratio (95% CI) Model 3		1.00 [ref]	0.31 (0.10-0.96)	0.52 (0.19- 1.44)	0.63 (0.36-1.11)

Data are presented as means (standard deviations) unless indicated otherwise. Data were analyzed with chi-square tests (categorical variables) or F-tests (continuous variables).

* 500 MET-minutes per week;

† current smoking (yes or no);

‡ >14 drinks per week;

§ Parental history of cardiovascular disease (yes or no);

// abnormal electrocardiogram (yes or no from resting or exercise ECG);

hypertension (yes or no from self-report or measured Blood Pressure $\geq 140/90$ mm Hg);

** diabetes (yes or no from self-report, taking insulin, or measured glucose ≥ 126 mg/dL);

†† only in the subsample with CRF data (n=7,669).

‡‡ Adjusted for age;

§§ Adjusted for Model 1 plus body mass index (kg/m^2), meeting aerobic physical activity guidelines (≥ 500 MET-minutes per week), current smoking, and heavy alcohol drinking (>14 drinks per week).

||| Adjusted for Model 2 plus parental history of cardiovascular disease, abnormal electrocardiogram, hypertension, and diabetes (all yes or no).

CI, confidence interval. CRF, cardiorespiratory fitness. CVD, cardiovascular disease.

Total muscular strength scores were standardized into z-scores using the sample's mean and standard deviation of their standardized total strength (combined bodyweight-adjusted leg and chest press) scores. Total muscular strength z-scores had a mean of 0 and a standard deviation of 1.