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Relationships between physiological stress biomarkers and cardiovascular disease risk factors among career firefighters

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Clinical Significance

Physiological stress is linked to cardiovascular disease (CVD) risk. Understanding this association provides insight into the allostatic load experienced by firefighters. Several non-conventional biomarkers may better predict CVD risk; thus, it is critical to understand the relationships between health and fitness parameters and these novel CVD risk biomarkers.

Abstract

Objective: The present study examined novel and classic CVD risk factors among career firefighters to understand better the associations between physiological stress, oxidative stress, inflammation biomarkers, and CVD risk. **Methods**: Associations between muscular and cardiorespiratory fitness (CRF) measures, body composition, physiological stress, and novel/classic CVD risk factors were assessed among 97 career male firefighters. **Results:** Muscular fitness/CRF, adiposity, body composition, and blood lipids were associated with CVD risk as measured by biomarkers for insulin resistance, inflammation, and oxidative stress**.** No associations between physiological stress biomarkers and CVD risk factors were found. **Conclusions**: Firefighters should improve their muscular fitness/CRF and body composition to reduce CVD risk.

Keywords: Firefighting, Heart Disease, Fitness, Cardiometabolic Health

SMART: Specific, Measurable, Achievable, Relevant, Time-Bound

- Physiological stress is often suggested as the underlying cause of cardiac-related deaths among firefighters; however, no data exist to demonstrate the relationship between stress and CVD risk among firefighters.
- Assessing the relationships between physiological stress and CVD risk provides valuable information about the allostatic load among firefighters.
- Improving and maintaining aspects of physical fitness and body composition measurements appear to be critical in reducing CVD risk.

1. Introduction

Since 1986, significant cardiac-related events (i.e., heart attacks) have accounted for ≈50% of on-duty fatalities among firefighters (1-3). Firefighting is arduous, exposing the firefighter to numerous stressors that induce cardiovascular strain, oxidative stress, chronic physiological stress and inflammation, and endothelial dysfunction. In addition, firefighters who lack appropriate physical fitness requirements and are classified as overweight or obese with poor health profiles often demonstrate reduced occupational performance and elevated risk for cardiovascular disease (CVD) (i.e., high concentrations of blood triglycerides [TAG], oxidative stress biomarkers, and low high-density lipoprotein cholesterol [HDL] concentrations) (4). Interestingly, Lockie and colleagues (5) reported that while 270 male and female career firefighters appear physically fit, they still demonstrate elevated CVD risk due to their poor body composition profiles (i.e., greater body mass index [BMI], waist circumference [WC], and waist-to-hip ratios [WHR]). A recent review has reported findings from several studies that indicate significant relationships between physical fitness metrics, occupational performance, and CVD risk (4). However, the role of stress biomarkers in CVD risk for firefighters is understudied.

Structural firefighting has been shown to yield high heart rate (HR) values (84-100% HR_{max}), peak blood lactate levels (6 to 13 mmol/L), and oxygen uptake values (i.e., $V\dot{O}_{2max}$) ranging between 39 to 45 ml/kg/min (6-9). Thus, it has been suggested that firefighters should have robust cardiorespiratory and anaerobic/muscular fitness to meet the physical demands of their occupation (10-12). Chizewski and colleagues (11) demonstrated that cardiorespiratory fitness (CRF), muscular endurance, and power were positively correlated with firefighter performance on an academy firefighting challenge, emphasizing the importance of obtaining and maintaining high

cardiorespiratory and muscular fitness levels. Norris et al. (13) showed that lower body strength and time to exhaustion (TTE) during a maximal cardiopulmonary exercise stress test (CPXT) were associated with work efficiency during simulated firefighting. Furthermore, firefighters with higher CRF and less central adiposity show lower levels of oxidative stress and inflammatory biomarkers (14-16). Recently, McAllister et al. (16) demonstrated that firefighters with greater CRF expressed lower concentrations of advanced oxidation protein products (AOPP) and C-reactive protein (CRP) than their lesser-fit counterparts. Further, McAllister and colleagues (15) found that AOPP and CRP concentrations were associated with TAG concentrations, TTE on a CPXT, WC, and body fat percentage (BF%) among structural firefighters. However, there is a paucity of data regarding physical fitness and physiological stress among firefighters.

Oxidative stress and inflammation play a key role in the development and progression of CVD, and while monitoring biomarkers, such as AOPP and CRP, may offer better insight into disease risk (15, 16), stress/overexertion is often suggested as the cause of the significant cardiac-related events experienced on duty (2, 3, 17-22). High-stress occupational conditions lead to increased physiological stress by activating the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adreno-medullary (SAM) axes, triggering the adrenergic fight-or-flight response, which is beneficial in the short term. However, chronic stress exposure may alter cardiovascular reactivity and increase oxidative stress, inflammation, and CVD risk. Therefore, it is plausible that monitoring physiological stress biomarkers may be useful in assessing or predicting CVD risk among firefighters. To date, only a handful of studies have assessed the physiological stress response to firefighting conditions (7, 18, 23-25). For instance, Gonzalez and colleagues (18) assessed the physiological stress response among 76 male structural firefighters, showing that

salivary α-amylase (AA), cortisol (CORT), and secretory immunoglobulin-A concentrations were significantly elevated immediately post-live fire suppression (94%, 91%, and 42% higher than baseline values, respectively). Perroni et al. (23) showed that 20 male firefighters engaging in fire-suppressive activities experienced a ≈174 and ≈109% increase in AA and CORT concentrations 30 minutes post-task, respectively. Waldman and colleagues (24) also found that firefighters performing a live-burn search and rescue task experienced a ≈150% and ≈57% increase in AA and CORT concentrations immediately post-task. Importantly, these findings provide insight into the amounts of physiological stress faced during live fire suppression; however, it remained unclear if the elevated physiological stress is directly related to markers of oxidative stress, inflammation, and CVD risk among firefighters.

Identifying fitness and health variables related to CVD risk can provide better assessment and monitoring methods among firefighters. While previous reports have demonstrated an inverse relationship between higher CRF and oxidative stress and inflammatory biomarkers, BF%, and girth measurements, no study has assessed the relationships between these factors and physiological stress biomarkers. Therefore, the purpose of this study was to examine the associations between biomarkers of physiological stress (AA and CORT) and various fitness and health parameters (i.e., CRF and muscular fitness metrics, body composition parameters, and blood CVD risk biomarkers) and oxidative stress (AOPP) and inflammatory (CRP) biomarkers.

2. Methods

2.1. Participants and Experimental Design

Ninety-seven career male firefighters from a local Fire Department (Bryan, Texas) were studied. Participants gave written, informed consent before completing a series of general health and lifestyle history questionnaires. The University Institutional Review Board approved all study procedures (IRB2023-0957D). Data collection occurred during Spring 2023 as part of an annual clinical evaluation program. Twenty-nine health and fitness parameters were assessed across five domains, including (1) fitness (TTE on a CPXT, push-ups, sit-ups, sit-and-reach), (2) body composition and anthropometrics (android/gynoid fat, fat and lean mass, BF%, WC, WHR, body mass), (3) conventional cardiometabolic health biomarkers (glucose, hemoglobin a1c [HbA1c], Homeostatic Model Assessment for Insulin Resistance [HOMA-IR], insulin, high-density lipoprotein cholesterol [HDL], low-density lipoprotein cholesterol [LDL], total cholesterol [TC], TAG, Apolipoprotein B [ApoB]), (4) and non-conventional biomarkers, such as physiological stress biomarkers (AA and blood and salivary CORT), and (5) inflammation/oxidative stress biomarkers (AOPP and CRP). Sample descriptive and demographic statistics are presented in **Table 1**.

2.2. Testing Procedures

The following testing procedures have been previously described (15, 16) and are part of a large annual clinical testing battery conducted for local first responders. All demographic, anthropometric, and body composition data were collected along with CRF and muscular fitness parameters and conventional/non-conventional blood and saliva biomarkers. Each portion of the annual clinical testing followed standard procedures (26). The participants completed two days of

testing, one of which was completed at the fire station. Before reporting to the station, the participants were instructed to observe a 12-hour overnight fast in preparation for a blood draw. The participants also donated a saliva biosample during this initial testing day. Next, the participants reported to the laboratory for the remaining clinical testing battery on a separate day. Upon arrival to the laboratory, each participant had their resting hemodynamic assessed, height and weight taken, and their waist and hip circumferences measured (which followed the World Health Organization standards) (27). The participants had their body composition assessed via a Dual-energy X-ray absorptiometry scan (DEXA; Hologic Horizon A, Marlborough, MA) and then completed a CXPT using the Bruce protocol using a standard TM65 treadmill and a 12-lead electrocardiogram system (Quinton Q Stress System, Cardiac Science Corporation, Bothell, WA]), where the Foster equation (28) was used to predict $V\dot{O}_{2max}$, factoring in TTE.

2.3. Blood Collection and Analysis Procedures

Fasting blood biosamples (≈8.5 mL) from the antecubital fossa following standard phlebotomy procedures were collected into 2 × 8.5 mL serum separation tubes (SST) and 1 × 4 mL K2 EDTA tubes (Becton, Dickinson and Company, Franklin Lakes, New Jersey) tubes (29). Then, the biosamples were allowed to rest and clot at room temperature for ≈30 minutes before being centrifuged for 15 minutes at 2500 revolutions/min at 4°C. One SST was immediately sent on ice to a commercial lab (Clinical Pathology Labs Inc., Austin, TX) to analyze TC, TAG, HDL, LDL, glucose, and ApoB. The second SST had serum aliquoted and stored at −80°C and later analyzed for insulin, AOPP, and CRP concentrations. The insulin, AOPPs, and CRP concentration analyses were conducted in duplicate using commercially available enzyme-linked immunosorbent assay (ELISA) kits: insulin (ALPCO, Salem, NH), CRP (R&D systems, Inc. Minneapolis, MN), blood

CORT (EagleBio, Amherst, NH), and AOPPs (Cell Biolabs, San Diego, CA) following the manufacturer instructions. Absorbance was detected via a BioTek colorimetric plate reader (Winooski, VT). Homeostatic Model Assessment for Insulin Resistance was calculated by fasting GLU (mg/dL) × fasting insulin (μU/mL)/405.

2.4. Saliva Collection and Analysis Procedures

Saliva biosamples were obtained via a passive drool collection method (Salimetrics, PA) previously used (18) and analyzed for concentrations of AA and CORT. Participants were instructed to mouth rinse with water prior to providing the saliva sample (≈10 minutes before biosample collection). The saliva biosamples were then transferred to a laboratory for storage at −80°C and later analyzed. Prior to analysis, the biosamples were thawed and centrifuged for 15 minutes at 1500 rpm at 4°C. Then, samples were analyzed in duplicate for AA and CORT concentrations using commercially available ELISA kits (Salimetrics, PA). Absorbance was detected via a BioTek plate reader (Winooski, VT). An automated washer was used to wash assays (BioTek, Winooski, VT). The intra-assay and inter-assay coefficients of variation were <10% for all assays.

2.5. Statistical Analysis

All analyses were conducted using the R statistical software (v4.3.3; R Core Team, 2024). The biomarkers AOPP, CRP, HOMA-IR, AA, and blood and salivary CORT were dependent variables in multivariate models. Initial models indicated the presence of multicollinearity among predictors (i.e., the remaining body composition, fitness, and cardiometabolic variables). Thus, dimension reduction using principal components analysis (PCA) was conducted to summarize variables along

dimensions that explained variance in the underlying data (i.e., using varimax rotations) within each variable group. Before PCA, all variables were log-transformed if they had a skew >1.0 and z-standardized (mean=0, SD=1). Following PCA, the top principal components (PCs) for each variable group were extracted and used to predict levels of the six key biomarkers using multiple regression, with and without statistically adjusting for age. Multiple comparisons were corrected using the false-discovery rate (FDR) method (30), with the family-wise error rate defined according to the six key dependent variables and age-adjustment status.

3. Results

Data were collected from all 97 participants and were winsorized at the 2nd/98th percentile (31). Despite this, some analytes had levels beyond the detection limits of specific assays, resulting in differing amounts of missingness. This results in the removal of observations noted in **Table 1** – particularly for TTE, sit-ups, push-ups, ApoB, Insulin, HbAlc, HOMA-IR, AA, blood/salivary CORT, AOPP, and CRP. Each model presented indicates the sample size represented.

3.1. Dimension reduction

3.1.1. Fitness Metrics

The fitness variables TTE, sit-ups, push-ups, and sit-and-reach were included in a PCA (**Table 2**), and a single PC with an eigenvalue >1.0 was extracted, explaining 55.6% of the variance in the data. This PC was interpreted as representing a "general fitness" dimension in the data, as the factor loadings were of similar magnitude for all variables (ranging from 0.5 to 0.59), except for sit-and-reach (loading = 0.33), indicating a smaller contribution of flexibility.

3.1.2. Body composition

Eight body composition variables (i.e., android and gynoid fat, fat mass, BF%, lean mass, WC, WHR, and body mass) were included in a second PCA, wherein two PCs with eigenvalues >1.0 were extracted. The first PC (65.7% variance explained) interpreted captured a "general adiposity" dimension in the data, with consistent small-moderate loadings across all variables (ranging from 0.24 to 0.43), except for WHR, which had a very small loading of 0.1. It should be noted that PC1 was reverse coded to ease interpretability—original loadings were all negative—so more positive loadings were associated with greater adiposity. The second PC (16.9% variance explained) provided more specificity in the pattern of loadings that were interpreted as targeting a dimension related to "lean mass/fat distribution." The two most substantial loadings were for lean mass (0.63) and gynoid fat percent (-0.44), with the other loadings below 0.35 in absolute value.

3.1.3. Cardiometabolic health

A final PCA included eight cardiometabolic health variables (i.e., HDL, LDL, TC, TAG, ApoB, Glucose, Insulin, and HbA1c), wherein three PCs with eigenvalues >1.0 were extracted. The first PC (explaining 45.5% of the variance) was interpreted as capturing associations along a general "lipid imbalance" dimension in the underlying data, with moderate factor loadings for LDL and TC, as well as TAG and ApoB (loadings were 0.48, 0.45, 0.37, and 0.47, respectively). It should be noted that PC1 was reverse-coded to ease interpretability, so positive values were associated with higher lipid values, save for HDL. The second PC (17.1% variance explained) was interpreted as capturing the dimension of "glucose control," with high factor loadings for glucose (0.69) and HbA1c (0.58). Finally, the third PC (13.5% variance explained) was interpreted as the "HDL" dimension, with a high loading for HDL (0.66) and a moderate loading for TAG (-0.47).

3.2. Multivariate analysis

Using the PCs for each variable group identified above, the key dependent variables were regressed on the group-specific PCs in individual models. All models were initially estimated without covariates, and then age was included in a second model to rule out age-related confounding. Since PCs have no natural unit, all estimates are reported as standardized regression coefficients. Findings are reported according to each group of predictors.

3.2.1. Fitness

Across models, general fitness (PC1 only) demonstrated a statistically significant association with HOMA-IR (b=-0.29, p=0.009) (**Table 3**). Though this association was robust to age adjustment (b=-0.29, p=0.012), the models explained only a small degree of variance in HOMA-IR (both R^2=0.08).

3.2.2. Body composition

General adiposity (PC1) demonstrated statistically significant positive associations with both HOMA-IR (b=0.46, p<0.001) and CRP (b=0.42, p<0.001) (**Table 4**), which were unchanged by the age-adjusted model. Additionally, the body composition PCs explained a small-moderate amount of variance in the HOMA-IR and CRP models (R^2 was 0.21 and 0.20, respectively, for the unadjusted models). Lean mass/fat distribution (PC2) was not associated with dependent variables across any model.

3.2.3. Cardiometabolic health

Lipid imbalance (PC1) was positively associated with both AOPP (b=0.55, p<0.001) and HOMA-IR (b=0.57, p<0.001) (**Table 5**). These associations were robust to the inclusion of age in the model (b_{AOPP}=0.56; $b_{HOMA\text{-}IR}$=0.59). After adjusting for age, lipid imbalance also demonstrated a small negative association with blood cortisol (b=-0.22, p=0.044); however, this association was not statistically significant after FDR adjustment. Glucose control (PC2) was positively associated with HOMA-IR (b=0.47, p<0.001) and was robustly associated when age-adjusted (b=0.48). Glucose control was also associated with AOPP (b=-0.15, p=0.04) and blood cortisol (b=0.26, p=0.026); however, these associations did not remain statistically significant after FDR adjustment. HDL (PC3) was negatively associated with AOPP (b=-0.51, p<0.001) and was not impacted by the inclusion of age in the model. Given these results, it is unsurprising that the PCs for cardiometabolic health explained a large amount of variance in the AOPP and HOMA-IR models (R^2s were 0.59 and 0.56, respectively, for the unadjusted models), and less variance for the blood cortisol model (R^2=0.11).

4. Discussion

The main findings of this study demonstrate that cardiorespiratory and muscular fitness, adiposity, body composition, and blood lipids are significantly associated with elevated biomarkers of insulin resistance, inflammation, and oxidative stress. These findings corroborate our previous work (15, 16), which suggests firefighters should maintain high CRF and muscular fitness and *healthy* body composition profiles (i.e., greater lean mass and lower fat mass and central adiposity) to reduce their CVD risk. Stress and overexertion have long been touted as the underlying culprit for premature mortality among firefighters (2, 3, 17, 19-22, 32, 33). Yet,

physiological stress biomarkers were not associated with any fitness or cardiometabolic health markers among this cohort of career firefighters. Blood CORT was positively associated with the PC for glucose control (i.e., higher glucose and HbA1c); however, this relationship did not survive the correction for multiple testing. In addition, sAA and sCORT were not associated with the fitness and health parameters. These findings indicate that firefighters should strive to maintain high cardiorespiratory and muscular fitness levels to enhance cardiometabolic health and that physiological stress biomarkers did not correlate with cardiometabolic health.

Firefighting is stressful and induces substantial metabolic and cardiovascular strain (32-36), which may largely be due to exposure to heat stress (19). Previous work by Webb and colleagues (32) demonstrated that firefighters participating exposed to concurrent stressors (i.e., carrying out physically and mentally demanding tasks) experience elevations in epinephrine, norepinephrine, and CORT concentrations, which were positively associated with inflammatory biomarkers (i.e., interleukin-6). Furthermore, Gonzalez et al. (35) and Perroni et al. (23) demonstrated that live fire search and rescue training evolutions increased physiological stress biomarkers, such as AA (≈94% and ≈174%, respectively) and CORT (≈91% and ≈109%, respectively). While these findings follow acute stress exposure scenarios, it is plausible that monitoring physiological stress biomarkers may offer valuable and mechanistic insight into firefighters' CVD risk. Given the common notion that CVD risk and premature mortality are linked to heightened stress among firefighters (10, 12, 17-22, 32, 33), we aimed to assess the relationship between basal levels of physiological stress biomarkers and other indices of CVD risk. However, the present data suggest no relationship between the physiological stress biomarkers and CVD risk parameters. These findings are incongruous considering the previous work demonstrating that

higher BF%, WCs, BMIs, and insulin resistance relate to elevated CORT levels (37-40). In addition, AA is generally considered an indicator of acute stress and may be better used to assess the stress response rather than monitoring for CVD risk (41). Presently, the state of the literature appears to be equivocal regarding the association between stress and CVD risk factors (i.e., metabolic syndrome) (42, 43). Thus, additional research is required to explore the associations between stress and CVD risk, especially among high-stress occupational groups, such as firefighters. Interestingly, there has been speculation that older firefighters may adapt to occupation-specific stressors, wherein they can deal with heat stress/strain better than their newer/younger counterparts (44). While the present findings do not suggest an impact of age on the relationship between physiological stress biomarkers and CVD risk parameters, this is an area warranting further exploration. Nevertheless, physiological stress biomarkers have been shown to vary greatly among first responder personnel (i.e., law enforcement) (45), and several biosamples over time likely need to be collected to assess and monitor the relationships between physiological stress and CVD risk.

Not surprisingly, increased adiposity was associated with high concentrations of HOMA-IR and CRP in the present study. Adipose tissue is known to secrete numerous cytokines that play a key role in facilitating inflammation and oxidative stress, resulting in a greater risk of insulin resistance and CVD (46). While CRP is considered a nonspecific inflammatory biomarker, concentrations are augmented in response to the secretion of other inflammatory cytokines (i.e., IL-6) (47, 48), particularly those related to atherosclerosis (49-52). Further, CRP has been implicated in vascular dysfunction and the development and progression of atherosclerosis (53-55). Previously, McAllister and colleagues (16) demonstrated that CRP was associated with higher

TAG concentrations, WCs, and BF%, as well as reduced CRF among career structural firefighters. Additionally, firefighters classified as having lower fitness based on the American College of Sports Medicine guidelines also showed higher CRP levels than their fitter counterparts (15). Interestingly, the present study did not identify associations between the general fitness PC and CRP; however, an inverse relationship was found between HOMA-IR and general fitness. Regular exercise can improve insulin sensitivity, fasting insulin, and blood glucose and, thus, lower HOMA-IR (56, 57). Unfortunately, data suggest that firefighters may become more physically inactive with age (58), which leads to a reduction in their CRF (15, 59, 60). Therefore, fire departments must consider implementing health programs focused on improving fitness (cardiorespiratory and muscular components) and other health components (i.e., body composition, biomarkers, etc.) (61-63). Taken together, firefighters should aim to increase their CRF and muscular fitness levels while improving their body composition (i.e., reducing fat mass and central adiposity while increasing lean mass) if they hope to better manage their CVD risk.

The PCs for lipid imbalance and glucose control were positively associated with AOPP and HOMA-IR but inversely associated with HDL, and these results were upheld when age-adjusted, except for the relationship between glucose control and AOPP. Blood lipid and glucose panels are routine for clinical assessment of cardiometabolic disease risk, and these findings corroborate our previous work that suggests elevated AOPP is associated with elevated blood lipids (15). Importantly, AOPP has been linked to atherosclerosis (64-66) and has been suggested as a predictive biomarker of CVD risk among firefighters (15, 16). In addition, some data suggest traditional biomarkers, such as blood lipids, may be insufficient in gauging CVD risk compared to oxidative stress and inflammatory biomarkers (67-69). Collectively, the present and previous

findings (15, 16) suggest that AOPP should be incorporated within annual CVD risk assessments, especially considering the role that oxidative stress plays in the progression of CVD (65, 67, 70).

The present study has limitations. First, data used in this study came from a convenience sample; thus, strict interpretations of inferential statistical tests are inappropriate. All statistical tests should be interpreted descriptively and understood relative to the current study's sample. Second, omitted variable bias can be viewed as a limitation of the present study. While the influence of age across models was accounted for, other dimensions (e.g., race/ethnicity and socioeconomic status) were not. Therefore, these known sources of variation in health may have impacted the results. Third, while only speculative, it is important to note the firefighters of this study undergo clinical testing on pre-determined testing dates, which are coordinated with the Assistant Fire Chief and Training Chief. Thus, some firefighters were tested when starting their shift, while others were tested following shift completion. It is plausible that the variation noted for the physiological stress biomarkers (i.e., large SDs) may be due to a variation in stressors that may occur on shift. Lastly, our sample did not include female firefighters based on who volunteered to participate; thus, future work should assess these relationships between sexes.

5. Conclusions

The present study suggests firefighters should improve their CRF and muscular fitness, body composition, and cardiometabolic health biomarker profiles (i.e., blood lipids and glucose) to lower their CVD risk. Firefighting is physically, mentally, and environmentally arduous, increasing oxidative stress, physiological stress, and inflammation exposure. Interestingly, these findings do not demonstrate a link between stress and traditional CVD risk factors; however,

multiple time points for the assessed biosamples are likely needed to better understand the association between stress and CVD risk. Nevertheless, the present study demonstrates the importance of exercise and nutritional interventions to improve CRF, muscular fitness, body composition, and cardiometabolic health. Future research is warranted to understand the etiology and progression of CVD among firefighters, especially over the career span and between sexes.

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Table 1. Sample descriptive and demographic.

	N	Mean	SD	Range
Demographics				
Age (years)	97	35	10	19 - 62
Body Composition				
Waist cir. (cm)	97	36.7	4.5	27.5 - 53.0
Waist-hip ratio	97	0.95	0.06	0.74 - 1.07
Weight (lbs)	97	208	34	142 - 360
Fat mass (%)	97	24.1	5.3	14.7 - 39.3
Fat mass (lbs)	97	52	19	22 - 131
Lean mass (lbs)	97	159	22	114 - 253
Android fat (%)	97	28	7	15 - 46
Gynoid fat (%)	97	25.5	4.6	16.6 - 37.7
Physical Fitness				
Time-to-exhaustion on CPXT (min)	96	10.97	1.60	6.70 - 15.33
Sit-ups (repetitions)	95	40	9	15 - 64
Push-ups (repetitions)	95	48	15	15 - 84
Sit-and-reach (inches)	97	14.4	3.5	6.0 - 25.7
Cardiometabolic Health				
HDL cholesterol (mg/dL)	97	49	11	29 - 82
LDL cholesterol (mg/dL)	97	124	29	58 - 189
Total cholesterol (mg/dL)	97	194	32	125 - 264
Triglycerides (mg/dL)	97	118	69	37 - 310
ApoB (mg/dL)	96	103	24	63 - 156
Glucose (mg/dL)	97	89	9	70 - 121
Insulin (μU/mL)	86	8.9	5.3	2.9 - 41.1
HbA1c (%)	96	5.44	0.25	4.84 - 6.00
HOMA-IR	86	1.97	1.20	0.57 - 8.84
Stress Markers				
a-amylase (U/mL)	74	62	46	3 - 206
Blood cortisol (μg/dL)	93	14.2	4.7	3.0 - 25.9
Salivary cortisol (μg/dL)	73	0.31	0.16	0.07 - 0.84
Inflammation & Oxidative Stress Markers				
AOPPs (μM)	93	130	72	57 - 346
CRP (ng/mL)	87	1,421	1,206	125 - 4,856

AOPPs = Advanced Oxidation Protein Products; ApoB = Apolipoprotein B; CPXT = maximal cardiopulmonary exercise test; CRP = C-Reactive Protein; HbAlc = Hemoglobin A1c; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein.

Table 2. Factor loadings of fitness and health variables across principal components, and their zero-order correlations.

		Principal Components			Pearson's r						
		PC 1	**PC 2**	**PC 3**	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Fitness											
1	Time-to-exhaustion on CPXT (min)	0.50	–	–	–						
2	Push-ups (repetitions)	0.59	–	–	0.51	–					
3	Sit-ups (repetitions)	0.55	–	–	0.38	0.71	–				
4	Sit-and-reach (Inches)	0.33	–	–	0.29	0.26	0.27	–			
% Variance Explained		55.6	–	–							
Body composition											
1	Android fat (%)	0.40	-0.24	–	–						
2	Gynoid fat (%)	0.35	-0.44	–	0.81	–					
3	Fat mass (lbs)*	0.43	-0.03	–	0.91	0.81	–				
4	Fat mass (%)	0.40	-0.29	–	0.95	0.91	0.93	–			
5	Lean mass (lbs)	0.24	0.63	–	0.26	0.12	0.54	0.23	–		
6	Waist circumference (cm)	0.39	0.17	–	0.79	0.57	0.85	0.75	0.56	–	
7	Waist-hip ratio	0.10	0.35	–	0.18	-0.06	0.18	0.16	0.13	0.32	–
8	Weight (lbs)*	0.38	0.34	–	0.66	0.53	0.88	0.66	0.84	0.82	0.17
% Variance Explained		65.7	16.9	–							
Cardiometabolic health											
1	HDL cholesterol (mg/dL)	-0.30	0.19	0.66	–						
2	LDL cholesterol (mg/dL)	0.48	-0.09	0.31	-0.31	–					
3	Total cholesterol (mg/dL)	0.45	-0.06	0.39	-0.13	0.93	–				
4	Triglycerides* (mg/dL)	0.37	-0.13	-0.47	-0.55	0.46	0.51	–			
5	ApoB (mg/dL)	0.47	-0.14	0.21	-0.40	0.90	0.81	0.55	–		
6	Glucose (mg/dL)	0.14	0.69	0.04	-0.07	0.17	0.13	0.09	0.19	–	
7	Insulin* (μU/mL)	0.29	0.32	-0.14	-0.25	0.36	0.37	0.35	0.36	0.37	–
8	HbA1c (%)	0.09	0.58	-0.15	-0.08	0.21	0.21	0.18	0.14	0.40	0.12
% Variance Explained		45.4	17.1	13.5							

*Natural log. Note: PC1 for body composition and cardiometabolic health were reverse scored to ease interpretation. HbAlc = Hemoglobin A1c; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein.

Table 3. Six key biomarkers regressed on principal components of fitness indicators with/without age-adjustment.

	AOPPs			HOMA-IR			**α**-amylase			CRP			Blood cortisol			Salivary cortisol		
	β [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*
Unadjusted																		
General fitness (PC1)	-0.20	0.106	0.064	-0.29**	0.107	0.009	0.22	0.118	0.073	-0.19	0.110	0.10	0.08	0.107	0.4	0.03	0.122	0.8
R^2	0.039			0.083			0.046			0.034			0.007			0.001		
Age Adjusted																		
General fitness (PC1)	-0.22	0.114	0.059	-0.29*	0.115	0.012	0.22	0.125	0.085	-0.18	0.121	0.13	0.10	0.116	0.4	-0.01	0.129	>0.9
R^2	0.042			0.083			0.047			0.034			0.009			0.009		
Number of Observations	88			82			70			82			88			69		

[1]*p<0.05; **p<0.01; ***p<0.001; [2]SE = Standard Error; AOPPs = Advanced Oxidation Protein Products; CRP = C-Reactive Protein; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance.

Table 4. Six key biomarkers regressed on principal components of body composition markers with/without age-adjustment.

	AOPPs			HOMA-IR			α-amylase			CRP			Blood cortisol			Salivary cortisol		
	β [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*
Unadjusted																		
General adiposity (PC1)	0.05	0.105	0.7	0.46***	0.097	<0.001	-0.07	0.118	0.6	0.42***	0.097	<0.001	-0.09	0.103	0.4	-0.04	0.118	0.8
Lean mass/fat dist. (PC2)	0.10	0.105	0.3	0.01	0.097	>0.9	-0.03	0.118	0.8	-0.14	0.097	0.2	-0.17	0.103	0.10	-0.14	0.118	0.2
R^2	0.012			0.212			0.005			0.203			0.037			0.021		
Age Adjusted																		
General adiposity (PC1)	0.03	0.107	0.8	0.46***	0.098	<0.001	-0.07	0.121	0.6	0.42***	0.100	<0.001	-0.10	0.105	0.4	-0.02	0.121	0.9
Lean mass/fat dist. (PC2)	0.11	0.105	0.3	0.01	0.098	>0.9	-0.03	0.119	0.8	-0.14	0.098	0.2	-0.17	0.104	0.11	-0.15	0.119	0.2
R^2	0.018			0.215			0.006			0.204			0.039			0.031		
Number of Observations	93			86			74			87			93			73		

[1]*p<0.05; **p<0.01; ***p<0.001; [2]SE = Standard Error; AOPPs = Advanced Oxidation Protein Products; CRP = C-Reactive Protein; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; "fat dist" = Fat Distribution.

Table 5. Six key biomarkers regressed on principal components of cardiometabolic health markers with/without age-adjustment.

	AOPPs			HOMA-IR			α-amylase			CRP			Blood cortisol			Salivary cortisol		
	β [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*	***β*** [1]	*SE*[2]	*p*
Unadjusted																		
Lipid imbalance (PC1)	0.55***	0.072	<0.001	0.57***	0.074	<0.001	-0.15	0.127	0.2	0.16	0.112	0.15	-0.20	0.105	0.067	-0.11	0.126	0.4
Glucose control (PC2)	-0.15*	0.072	0.040[†]	0.47***	0.074	<0.001	-0.05	0.126	0.7	0.11	0.112	0.3	0.26*	0.105	0.016[†]	0.15	0.126	0.2
HDL cholesterol (PC3)	-0.51***	0.072	<0.001	-0.13	0.074	0.094	0.01	0.127	>0.9	0.01	0.112	0.9	0.04	0.105	0.7	-0.02	0.126	0.9
R^2	0.584			0.558			0.026			0.038			0.106			0.037		
Age-Adjusted																		
Lipid imbalance (PC1)	0.56***	0.074	<0.001	0.59***	0.076	<0.001	-0.17	0.130	0.2	0.17	0.117	0.15	-0.22*	0.108	0.044[†]	-0.11	0.129	0.4
Glucose control (PC2)	-0.14	0.072	0.051	0.48***	0.074	<0.001	-0.06	0.129	0.6	0.11	0.113	0.3	0.24*	0.106	0.023[†]	0.16	0.128	0.2
HDL cholesterol (PC3)	-0.51***	0.072	<0.001	-0.12	0.074	0.11	0.02	0.128	>0.9	0.02	0.113	0.9	0.04	0.105	0.7	-0.02	0.128	0.9
R^2	0.587			0.568			0.032			0.039			0.117			0.039		
Number of Observations	85			85			65			81			85			65		

[1]*p<0.05; **p<0.01; ***p<0.001; [2]SE = Standard Error; [†]*P*>0.05 after FDR correction; AOPPs = Advanced Oxidation Protein Products; CRP = C-Reactive Protein; HOMA-IR = Homeostatic Model Assessment of Insulin Resistance; HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein.