Relationships between cardiorespiratory and muscular fitness with cardiometabolic risk in adolescents.

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Abstract

This study examined the independent relationships between cardiorespiratory and muscular fitness with cardiometabolic risk in adolescents. Subjects were 192 adolescents (118 boys), aged 15 – 17.5 years. The 20 m multi-stage fitness test assessed cardiorespiratory fitness and the counter movement jump assessed muscular fitness. Additional measures included interleukin-6, C-reactive protein, adiponectin, fibrinogen and plasminogen activator inhibitor-1. Regression analysis revealed that cardiorespiratory fitness was negatively related to cardiometabolic risk (β = -0.014, $p < 0.001$). With additional adjustment for muscular fitness the relationship remained significant **(β = -0.015,** $p < 0.001$). Muscular fitness was negatively related to cardiometabolic risk (β = -0.021, $p < 0.001$) and remained significant after adjustment for cardiorespiratory fitness. Participants in the least-fit quartile for both cardiorespiratory and muscular fitness had significantly poorer cardiometabolic risk scores than those in the other quartiles. Findings revealed that muscular and cardiorespiratory fitness are significantly associated with cardiometabolic risk independently of one another.

Key words: Cardiorespiratory fitness, muscular fitness, inflammation, adolescents.

Introduction:

Although prediction of cardiometabolic risk was once considered only pertinent to adults, it is now accepted as a paediatric problem since the pathological processes begin in childhood (Daniels, Pratt, & Hayman, 2011). The clustering of risk factors such as insulin resistance, elevated triglyceride concentrations, central obesity, low cardiorespiratory fitness (CRF), physical inactivity and low high-density lipoprotein (HDL) concentrations are routinely noted among both children and adolescents (Anderssen et al., 2007). Whilst there may be a genetic predisposition to some of these risk factors in certain individuals, most develop as a result of unhealthy lifestyle choices often beginning in childhood that lead to excess adiposity, physical inactivity and consequently low CRF (Cook et al., 2000; Valle et al., 2005). Understandably there is an increasing desire to interpret the pathophysiological process which underpins cardiometabolic risk and indeed the interplay between risk factors associated with this disease, especially as early detection may help identify individuals in most need of intervention.

Once considered a simple storage depot for excess energy, adipose tissue has been identified as a complex endocrine organ that secretes a number of molecules involved in the regulation of many metabolic and hormonal signals in humans (Kahn & Flier, 2000). A number of inflammatory factors including adipokines or adipocytokines, secreted in response to increasing adipose tissue, are known to play an important role in the atherosclerotic process and the development of diabetes and hypertension. They can also predict future cardiovascular events (Daniels et al., 2011). Elevated levels of C-reactive protein (CRP) and interleukin-6 (IL-6) together with hypoadiponectinemia are present in obese children (Cook et al., 2000; Valle et al., 2005) and may demonstrate a plausible mechanism linking increased adiposity to the development of insulin resistance (IR), type 2 diabetes and cardiometabolic disorders. Moreover, an increasing evidence base has also established a strong connection between cardiomeatbolic risk, inflammation and thrombosis in adults (McDermott et al., 2003).

Fibrinogen is an independent risk factor for cardiovascular disease and is known to promote atherogenesis and thrombogenesis (Green, Foiles, Chan, Schreiner, & Liu, 2009) whereas plasminogen activator inhibitor-1 (PAI-1) whilst known to be associated with an increased risk of cardiometabolic disease and type 2 diabetes, also reduces blood fibrinolytic activity (hypofibrinolysis) (Alessi, Poggi, & Juhan-Vague, 2007). Evidence has demonstrated strong associations between fibrinogen, PAI-1, obesity and physical activity (Sola et al., 2007) but little is known of the relationships between measures of physical fitness. Yet, whilst obesity is a risk factor for insulin resistance, type 2 diabetes and cardiometabolic disease, not every obese individual is insulin resistant, or indeed at high risk for the development of diabetes and cardiometabolic disease (Karelis et al., 2005). Thus, identifying measures that can be targeted to improve cardiometabolic risk profiles is an important step in the promotion of health and well-being in youth.

Health related physical fitness is an important component of overall health and well-being in youth populations (Ortega, Ruiz, Castillo, & Sjostrom, 2008; Ruiz et al., 2009), and contains the following components: body composition, flexibility, cardiorespiratory fitness (CRF), and muscular fitness comprised of: strength, power and endurance (American College of Sports Medicine, 2013). Whilst all of these components are important attributes of good health, CRF has received the most attention in the literature as its measurement provides a useful indicator for assessing both symptomatic and asymptomatic individuals. Conclusive evidence shows that high levels of CRF can reduce the risk of all cause and early mortality in adults, independent of age, ethnicity, adiposity and smoking (Gulati et al., 2005; Lee et al., 2011) whilst also being inversely related to a reduced cardiometabolic risk profile in both children and adolescents (Anderssen et al., 2007; Hurtig-Wennlof, Ruiz, Harro, & Sjostrom, 2007).

Whilst CRF is considered a strong predictor for the clustering of cardiometabolic risk factors, recent investigations have also begun to explore the utility of other components of physical fitness such as measures of muscular fitness as an additional predictor (Artero et al., 2011; Steene-Johannessen, Anderssen, Kolle, & Andersen, 2009).

Recently, low muscular fitness levels have been linked to early mortality **(Ruiz et al., 2008).** Nonetheless, few studies have examined the independent relationships between muscular fitness, cardiorespiratory fitness and cardiometabolic risk in adolescents. Furthermore, to the best of our knowledge no study has yet to examine the interplay between measures of physical fitness with a composite cardiometabolic risk score which includes markers of inflammation and thrombosis in adolescents. Since evidence appears to indicate that cardiometabolic risk can track from adolescence into adulthood (Eisenmann, Welk, Wickel, & Blair, 2004), it is important that preventive strategies are implemented prior to adulthood. **We hypothesized that greater levels of CRF and muscular fitness would positively influence the cardiomeatbolic risk scores evident within this adolescent cohort.** Therefore, the purpose of this study was to establish the independent relationships between CRF, muscular fitness and cardiometabolic risk in healthy adolescents.

Methods

A cross-sectional sample of participants (118 boys, 74 girls, 16.73 ± 0.6 years) was recruited from schools in the West of Scotland. Prior to data collection, informed consent was obtained from all students and their parents and all were fully familiarised with testing and data collection procedures. The study was approved by the ethics committee of the University of the West of Scotland. All tests were performed between 9:00 am and noon and were conducted by the same individuals.

Barefoot stature was measured to the nearest 1 mm (Seca Stadiometer, Seca Ltd, Birmingham, UK). Weight in light indoor clothing, without shoes, was measured to the nearest 0.1 kg using calibrated electronic weighing scales (Seca 880, Digital Scales, Seca Ltd, Birmingham, UK). Body mass index (BMI) was calculated (weight/height^2, kg/m^2). Waist circumference (WC) was measured at the level midway between the lower ribs and iliac crest (Ledoux, Lambert, Reeder, & Despres, 1997). Sexual maturation status was self-assessed using the criteria for pubic hair (Tanner & Whitehouse, 1976) which has been shown to demonstrate predictive and discriminate validity of self-assessments when compared against physician Tanner ratings in youth (Schmitz et al., 2004).

CRF was measured using the 20 m multi stage fitness test (20MSFT, number of completed shuttles). Specific details of the 20MSFT protocol has been described elsewhere (Buchan et al., 2013). Participants ran in small groups of between 12 - 15 and were instructed to run between two lines 20m apart, whilst keeping pace with audio signals emitted from a pre-recorded CD and until exhaustion. **When participants could no longer keep up the pace by reaching the line at the time of the audio signal, participation was terminated and the number of laps completed was recorded.** Verbal encouragement was given throughout the test.

The counter movement jump (CMJ) test was used to measure lower-limb explosive muscular strength as a reliable estimate of muscular fitness (Ruiz et al., 2006) . For the remainder of the article, CMJ will be used to reflect muscular fitness unless otherwise stated. Jumping height was measured using the Optojump system (Microgate, Bolzano, Italy) after a standardized warm up. Participants were instructed to begin in a standing position with their feet shoulder width apart. Thereafter, they were instructed to perform a counter – movement with their legs prior to jumping. Each participant was instructed to perform three jumps with a minimum of two minutes recovery between each effort. The best of the three jumps (to the nearest cm) was used as the criterion measure. Participants were instructed to keep their hands on their hips throughout all jumps, to exert a maximal effort and land in an extended position.

Participants also completed a validated physical activity questionnaire for adolescents (PAQ-A) (Kowalski, Crocker, & Kowalski, 1997) which required them to recall their activity behaviours from the previous 7 days. Completed questionnaires were inspected and if necessary, clarification of responses was confirmed with participants.

Blood samples were taken between 9:00 and 11:00 am after an overnight fast. Fasting was verified prior to sampling. Qualified phlebotomists, experienced in paediatric sampling techniques collected all blood samples. Blood samples were obtained from an antecubital vein and collected in a BD Vacutainer plasma tube (Becton, Dickinson and Company, Franklin Lakes, USA). Plasma was isolated by centrifugation at 3,500 rpm for 10 minutes and frozen at -80^{o}C within two hours of collection. Analyses were completed within three months of collection. CRP, IL-6, adiponectin, fibrinogen and PAI-1 were measured using standard procedures. **Fibrinogen concentration was analysed using commercially available immunoassay kits (ALPCO,Salem, NH) and a MRX microplate reader (Dynatech Laboratories,MA). Concentrations of IL-6, CRP, adiponectin, and PAI-1 were measured with specific ELISA kits (R&D Systems, Abingdon, UK) and a MRX microplate reader (Dynatech Laboratories, MA).**

A continuous score representing a composite cardiometabolic risk score was constructed using the following variables: IL-6, PAI-1, CRP, adiponectin (inverted) and fibrinogen. Each variable was standardized as follows: standardized value = value-mean/SD, separately for boys and girls. The z-scores of the individual risk factors were then summed to create a clustered cardiometabolic risk score for each participant with a lower score indicating a healthier overall risk profile.

All analysis was undertaken using Statistical Package for the Social Sciences (version 18; SPSS Inc., Chicago, IL, USA), with values of $p < 0.05$ considered statistically significant. Descriptive data are presented as means and standard deviations where appropriate. Data was checked for normality of distribution before the analyses. Significant differences between the sexes were determined using independent t-tests or where appropriate, the Mann-Whitney (*U*) test. Differences in maturation status and physical activity were analysed using the chi-squared test.

Multiple regression analysis was used to examine the relationships between cardiorespiratory fitness (CRF), muscular fitness and the composite cardiometabolic risk score through two separate models. Model 1 included either CRF or muscular fitness with cardiometabolic risk and was adjusted for sex, age, physical activity, WC and pubertal status. In model 2, we additionally adjusted for the other predictor variable to determine whether independent relationships existed. **Since it is recommended that a sample size of 80 is suffice with up to 20 predictors to find a large effect (r = 0.5) (Miles & Shevlin, 2001), we are confident that the sample size is appropriate.** Finally, analysis of covariance (ANCOVA) was used to test differences in clustered cardiometabolic risk score across the different muscular fitness and cardiorespiratory fitness groups whilst controlling for sex, age, physical activity, maturation status, WC and the other independent variable.

Results

Participant characteristics are presented in table 1. Boys were taller ($p = 0.01$) and heavier ($p < 0.001$) than girls. Boys had higher CRF and muscular fitness as well as a greater WC than girls ($P = 0.018$). In addition, girls had a greater level of fibrinogen ($p < 0.001$) than boys. The multiple regression analysis (Table 2) revealed that CRF was negatively related to cardiometabolic risk ($\beta = -0.014$, $p < 0.001$) after adjustment for age, sex, WC, physical activity and maturation status (model 1). With the additional adjustment for muscular fitness in model 2, the relationship remained significant, albeit weak (**$\beta = -0.015$,** $p < 0.001$). When examining the relationships for muscular fitness, model 1 revealed muscular fitness was negatively related to cardiometabolic risk ($\beta = -0.021$, $p < 0.001$) after adjustment for age, sex, WC, physical activity and maturation status. With the additional adjustment for CRF in model 2, the relationships remained significant but weak ($\beta = -0.102$, $p < 0.001$). **In general the significance of the change in R^2 values in both model 1 and 2 when either CRF or muscular fitness was added confirmed each variables independent contribution.**

Figure 1 displays the composite cardiometabolic risk score by quartiles of CRF. The ANCOVA revealed significant differences between groups in composite cardiometabolic risk ($F = 4.80$, $P = 0.030$). *Post hoc* analysis revealed that participants in the lowest quartile of cardiorespiratory fitness had a significantly higher composite cardiometabolic risk score compared with all other quartiles ($P < 0.05$). No significant difference was found between the other cardiorespiratory fitness groups. Similarly, figure 2 displays the composite cardiometabolic risk score by quartiles of muscular fitness. The ANCOVA revealed significant differences between groups in composite cardiometabolic risk ($F = 7.39$, $P < 0.001$). *Post hoc* analysis revealed that participants in the lowest quartile of muscular fitness had a significantly higher composite cardiometabolic risk score compared with those in the third and fourth quartiles ($P < 0.05$). No other significant differences were evident.

Discussion

To the best of our knowledge, this is the first study to investigate the independent relationships between both CRF and muscular fitness with a composite risk score constructed from markers of inflammation and thrombosis. Our findings revealed that CRF and muscular fitness were related with the composite risk score, independently of one another. Previous investigations involving youth have consistently found significant negative relationships for CRF and cardiometabolic risk (Anderssen et al., 2007; Hurtig-Wennlof et al., 2007) and likely represents the benefits of increasing CRF upon both cardiovascular and metabolic function. In the study by Anderssen et al, (2007) the authors examined the cardiorespiratory fitness levels of nearly 3000 European youth aged either 9 or 15 years and found that those within the lowest quintile of fitness in comparison to those in the highest, were 13 times as likely to have clustering of traditional CVD risk factors (total cholesterol/high-density lipoprotein cholesterol ratio, plasma triglycerides, insulin resistance (homeostasis model assessment), sum of four skinfolds, and systolic blood pressure).

Unlike the study by Anderseen and colleagues, others (Artero et al., 2011; Martinez-Gomez et al., 2011; Steene-Johannessen et al., 2009) have also examined the relationship between CRF and cardiometabolic risk whilst controlling for muscular fitness. Collectively these authors have demonstrated that CRF was associated with cardiometabolic risk, independent of muscular fitness. Since our analysis controlled for pubertal stage, we are confident that this apparent protective effect of muscular fitness upon cardiometabolic risk is a result of participating in muscle strengthening activities rather than a consequence of maturation. As seen in other studies (Artero et al., 2011; Martinez-Gomez et al., 2011), we found that CRF appeared to be more strongly related to cardiometabolic risk in comparison to muscular fitness which may suggest that CRF is more important than muscular fitness in predicting cardiometabolic risk at least during adolescence. **Nonetheless, future work that considers implementing prospective and intervention study designs are needed to determine the independent influence of muscular fitness and CRF upon cardiometabolic disease risk in adolescents.**

The presence of sub-clinical inflammation is known to thicken blood vessels and damage pancreatic islet cells in diabetes and has been linked with chronic conditions such as type 2 diabetes and cardiometabolic disease (Ouchi, Parker, Lugus, & Walsh, 2011). Whether the obesity-related inflammatory state is linked to the development of cardiometabolic disease in youth however remains to be fully elucidated. Since obesity can often be the most visible indicator of an underlying disease condition it is not surprising that the focus of research has often centred on examining the relationships with obesity and variables linked to cardiometabolic disease, with subsequent preventative strategies then devised around reducing adiposity. However, our findings appear to suggest that both CRF and muscular fitness are independently related to cardiometabolic risk which may indicate that factors other than obesity could play a role in the development of adverse risk profiles. This is especially true since we were able to control **for waist circumference within our analysis.**

Across incremental groups for both CRF and muscular fitness (Figures 1 and 2), we demonstrated that participants in the first quartile (lowest cardiorespiratory and muscular fitness) had significantly greater cardiometabolic risk scores than those in other quartiles. Our findings are in agreement with others (Artero et al., 2011; Steene-Johannessen et al., 2009) who have demonstrated similar finding's.

The strength of this study is the measurement of markers of inflammation and thrombosis and the use of two measures of physical fitness in this cohort. By examining the relationships between physical fitness measures and cardiometabolic risk scores that encompass metabolic, inflammatory and thrombosis markers we have established that both CRF and muscular fitness are significantly, and independently, related to an increased risk profile. These findings add to the limited body of literature that has examined the interaction between CRF and muscular fitness and supports current recommendations (Department of Health, 2011; US Department of Health and Human Services, 2008) for minimising the occurrence of unhealthy risk profiles.

There are a number of limitations to this study. The observations of this study are limited by its cross-sectional design which does not allow us to establish definitive causality. The composite cardiometabolic risk score was estimated using a range of variables given equal weighting and are sample specific. Nonetheless, the use of a composite score is becoming a recognized method to examine and understand relationships in paediatric research (Artero et al., 2013). Finally, the methods used to assess CRF were field based but despite this, the 20 MSFT has been described as a valid and reliable method of estimating fitness in children and adolescents, and is widely used (Buchan et al., 2013).

Conclusion

Both muscular fitness and CRF are significantly and negatively associated with cardiometabolic risk, independently of one another. The results indicate that improvements in physical fitness are associated with a potential protective role on cardiometabolic risk in adolescents. Finally, our findings support the current physical activity recommendations for youth which recommend regular bone and muscle strengthening activities. Practitioners should consider implementing strategies that will enhance not only CRF, but also improve muscular fitness.

The authors declare they have no conflict of interest.

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