Impact of Physical Activity on Adiposity and Risk Markers for Cardiovascular and Metabolic Disease

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Abstract
The main aim of the present study was to investigate the impact of physical activity (PA) on adiposity and for cardiovascular and metabolic disease risk markers (CMDRMs). In total, 55 adults (33 lean [L] and 22 overweight/obesity [O/O]) visited the laboratory on two occasions. During the first session, body composition and anthropometric measurements were taken as well as resting blood pressure (BP). Free-living PA intensity was monitored using an ActiGraph accelerometer, which the participants wore for a period of 6 days. During the second visit, blood samples for the analysis of disease risk markers were obtained from the participants in the morning after overnight fasting (≥10 hr). There was no significant difference between groups in the percentage of time spent in PA levels (54.5% ± 1.2% and 54.9% ± 2.1% for L and O/O, respectively). Although, the O/O group was within recommended PA level, they had higher leptin, insulin, homeostatic model assessment of insulin resistance (HOMA-IR), and high-sensitivity C-reactive protein (hsCRP) levels than the L group (all \( p < .01 \)). The O/O group had higher levels of triglycerides, low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) and lower levels of high-density lipoprotein (HDL) (all \( p < .01 \)). Interestingly, vigorous activity was positively correlated with HDL (\( r = .30, p < .05 \)) and negatively with LDL (\( r = -.26, p = .05 \)) levels and the arachidonic acid to eicosapentaenoic acid (ARA/EPA) ratio (\( r = -.30, p < .05 \)). Only the O/O group had elevated CMDRMs. However, vigorous activity may improve health-related blood lipids such as HDL, LDL, and ARA/EPA ratio. Regardless of body composition status, low active participants were more likely to have higher level of leptin and hsCRP. Further exploration of the beneficial effects of vigorous exercise on adiposity and CMDRMs is warranted.

Keywords
physical activity, cardiovascular disease, adiposity, cytokine

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Introduction
Being physically active can reduce the risk of several metabolic diseases and certain types of cancer (Edmunds et al., 2020; Farrell et al., 2007) as well as lower the risk of morbidity and mortality, even among adults with obesity (Azeem & Antony, 2018; Blair & Brodney, 2001).

The associations between body fat percentage and physical activity (PA) status, on one hand, and cardiovascular and metabolic disease risk markers (CMDRMs); including the newer markers, such as high-sensitivity C-reactive protein [hsCRP], interleukin [IL]-6, tumor necrosis factor-alpha [TNF-α], leptin, and adiponectin, on the other hand, have been investigated using different subjective measurements (Cho et al., 2009; Monzillo...
et al., 2003). However, there is a lack of studies examining the effect of high and low PA status measured using objective methods, such as accelerometry, on CMDRMs, such as adiponectin, leptin, IL-6, hsCRP, and TNF-α. The present study might help shed light on the association between CMDRMs and PA status in adults and in turn contribute to improving the PA recommendations for adults. The present study therefore aimed to investigate the impact of PA on adiposity and CMDRMs.

Materials and Methods

Participants

In total, 55 adults, 18 to 55 years old, 33 lean (L; men = 15, women = 18) and 22 (men = 12, women = 10) with overweight/obesity [O/O], visited the laboratory on two occasions. In the first visit, we recorded body mass, height, body mass index (BMI), body fat, and resting heart rate and blood pressure. The participants were classified as L or O/O based on the BMI classification method of the American College of Sports Medicine guidelines (L, BMI < 25 kg/m²; O/O, BMI ≥ 25 kg/m²; Haskell et al., 2007). The participants then visited the laboratory in the morning after overnight fasting (≥10 hr) to provide a resting venous blood sample (10 mL) for the analysis of CMDRMs. The present study had been approved from the research ethics committee at the University of [ ] and from the research ethics committee of [ ]. All eligible participants were asked to sign a consent sheet.

Habitual PA Assessment

Free-living PA intensity was monitored using an accelerometer (ActiGraph GT1M) from Manufacturing Technology Inc. (ActiGraph, LLC, Fort Walton Beach, FL, USA), and PA levels were assessed over 6 consecutive days. The participants were asked to wear the ActiGraph for at least 10 hr of waking time each day.

Blood Samples

All blood samples were collected from an antecubital vein by a trained individual. Enzyme-linked immunosorbent assay was used to determine the leptin, adiponectin, TNF-α, hsCRP, IL-6, and insulin levels. The enzymatic assay procedures were used to determine triglyceride, total cholesterol, free fatty acid, and glucose levels. We examined the arachidonic acid to eicosapentaenoic acid (ARA/EPA) ratio, also known as (20:4n – 6)/(20:5n – 3), and the ratio of percentage n – 3 to total highly unsaturated fatty acids (HUFA) using the Ideal Omega Test available online (Test, 2010).

Data Analysis and Statistics

The statistical analysis was conducted using SPSS software for Windows (SPSS Inc., Chicago, IL, USA). An alpha (p) level of .05 was used for all analyses to indicate statistical significance. Data were summarized as mean differences with 95% confidence intervals (95% CIs) and as means and standard deviations (±SD). Independent-sample t tests were used to compare the measurements of CMDRMs and body composition for the L and O/O groups and between the active and sedentary groups. Pearson’s correlation coefficients were used to assess the strength of the relationship between CMDRMs and body composition.

Results

CMDRMs and PA Status

In total, 47 participants completed all parts of the study and were assigned to two groups based on their PA levels (high activity [HA] ≥ 300 min/week of moderate-to-vigorous physical activity [MVPA], and low activity [LA] < 150 min/week of MVPA; 22 to HA, 25 to LA).

There were significant differences between the two groups in terms of BMI (24.2 ± 3.4 and 26.9 ± 4.8 for HA and LA, respectively; p < .05), body fat percentage (22.4% ± 7.4% and 31.1% ± 12.8%; p < .01), mean arterial pressure (MAP; 87.0 ± 7.1 and 92.5 ± 10.3 mm Hg; p < .05), and diastolic blood pressure (DBP; 73.2 ± 8.0 and 84.6 ± 6.2 mm Hg; p < .05).

There were significant increases in leptin and hsCRP levels in the LA group compared with the HA group (Figure 1). The other blood markers showed no significant differences between the HA and LA groups.

Although the MAP and DBP levels were significantly higher in the LA group than in the HA group (p < .05), all blood pressure measurements for both groups were within the normal levels (Figure 2).

CMDRMs and Body Composition

Table 1 summarizes the participants’ physical characteristics. Table 2 lists the accelerometry data as M ± SD. The recorded times were significantly different between the L and O/O groups (p = .03). To normalize the compared values, the PA status variables were reported as the percentage of time spent at each PA level. The data in Table 2 show no differences between the L and O/O groups in the percentage of recorded time spent in sedentary and PA levels. Moreover, there were no significant intergroup differences in the percentage of active time spent at each PA level (all p > .05), although the results were almost statistically significant for vigorous activity...
Figure 1. Mean (±SD) Leptin and High-Sensitivity C-Reactive Protein (hsCRP) Levels of 47 Adults (22 High Activity and 25 Low Activity).

Note. SD = standard deviation; hsCRP = high-sensitivity C-reactive protein.
Intergroup differences are significant at *p < .05 and **p < .01.

Figure 2. Mean (±SD) Blood Pressure (Systolic, Diastolic, and Mean Arterial Pressure) of 47 Adults (22 High Activity and 25 Low Activity).

Note. SD = standard deviations.
Intergroup differences are significant at *p < .05.

Furthermore, certain cytokine markers (leptin and hsCRP) were significantly elevated in the O/O group compared with the L group (p < .01; Figure 4). Other markers (adiponectin, IL-6, and TNF-α) showed no differences (p = .92, p = .95, and p = .37, respectively).

The results of the insulin and homeostatic model assessment of insulin resistance (HOMA-IR) were
significantly higher in the O/O group than in the L group ($p < .01$; Figure 5), whereas fasting glucose levels showed no intergroup differences ($p = .85$).

There were statistically significant intergroup differences in the blood pressure measurements ($p < .01$). However, the mean blood pressure values were within the normal levels for both groups.

**Associations Between PA Intensity, Adiposity, and CMDRMs**

We used Pearson’s correlation analysis to examine the associations among PA intensity, body composition, and CMDRMs. The results indicated that HDL levels were positively correlated with vigorous PA intensity ($r = .27, p = .049$). Fasting glucose levels were inversely correlated with the percentage of time spent in MVPA intensity ($r = -.26, p = .053$). For fatty acids, the $n-6/n-3$ ratio was inversely correlated with vigorous and highly vigorous PA intensity ($r = -.30, p = .03$).

There was a moderately inverse correlation between HDL levels and weight ($r = -.39, p = .004$) and a moderately positive correlation between HDL levels and fat-free mass (FFM; $r = .39, p = .003$). VLDL levels had a moderate correlation with BMI ($r = .33, p = .041$). The percentage $n-3$ HUFA score was inversely correlated with FFM ($r = -.29, p = .045$). Adiponectin levels were correlated with FFM ($r = -.46, p < .001$), and leptin levels were positively correlated with body mass, BMI, and body fat percentage ($r = .55, r = .76$, and $r = .83$, respectively, all $p < .001$). Plasma hsCRP levels had a moderate correlation with body weight, BMI, and body fat percentage ($r = .36, p = .01; r = .46, p < .001$; and $r = .49, p < .001$, respectively).
Significantly higher in women (n=28) than in men (n=27; p < .001) in the present study. According to a recent study, the leptin/adiponectin ratio was lower in men than in women (p < .001; Selthofer-Relatić et al., 2018).

These results might be affected by sex more than by body fat percentage (Rak et al., 2017).

Plasma leptin has been known as a predictor of coronary heart disease (Keller et al., 2003; Zhao et al., 2021). The present study found that plasma leptin was significantly higher in the O/O group than in the L group (p < .01) and also associated with body weight, BMI, and body fat percentage (p < .001). Increased body adiposity might therefore increase the risk of cardiovascular and metabolic diseases even in apparently healthy adults with O/O and low PA, particularly when combined with other related CMDRMs, such as hsCRP, LDL, and VLDL.

Adults with obesity are at risk of developing CRP concentration which is recognized as an independent risk marker for cardiovascular disease (CVD; Ridker et al., 2002; Speer et al., 2021). The results of the present study showed that hsCRP levels were significantly influenced by body fat (p < .01), which corroborates the findings of a previous study (Monzillo et al., 2003). Ridker et al. (2002) developed an hsCRP risk range from 5,000 apparently healthy adults and suggested that hsCRP levels ≥ 2.0 µg/ml should be considered high. The authors suggested that elevated CRP levels with high total cholesterol-to-HDL cholesterol (TC: HDL-C) ratios represent a very high risk for CVDs for both men and women (Ridker et al., 2002). In the present study, the O/O group had a significantly higher hsCRP level (2.64 ± 0.42 µg/ml) and TC is to HDL-C ratio (1.13 ± 0.21 µg/ml). In addition, elevated hsCRP levels have been found to be associated with insulin resistance (Lemieux et al., 2001). Similar results were found in the present study, given that the O/O group had high levels of insulin and HOMA-IR. Thus, obesity might play a role in increasing hsCRP levels, which might be considered an independent CMDRM.

Although insulin levels for both groups were within the normal range, the participants in the O/O group might be at risk, especially when other risk markers, such as leptin and hsCRP, are present at high levels.

Plasma IL-6 levels were not significantly different between the L and O/O groups (p = .95) and were within the normal range (0.6–20 pg/ml), whereas other studies have found that plasma IL-6 levels decreased significantly after body weight reductions in adults with obesity (Monzillo et al., 2003). More research is therefore needed to examine the effect of body composition on plasma IL-6 levels, which have been identified as a risk predictor for myocardial infarction (Li et al., 2021). In the present study, no significant differences were found between the L and O/O groups in terms of plasma TNF-α levels. Although one study reported that TNF-α levels were elevated in adults with obesity (Hotamisligil et al., 1995), other studies have found no association between TNF-α
levels and obesity (Berggren et al., 2005). Similar to IL-6, TNF-α might be influenced more by various factors such as diet and PA (Hayase et al., 2002). Thus, the association between TNF-α and body composition might need further investigation.

**PA Status and CMDRMs in Adults**

The present study reported that DBP and MAP were significantly lower in the HA group than the LA group. Time spent doing vigorous PA was significantly higher in the HA group than in the LA group. Interestingly, vigorous activity may play role in improving blood lipids. For instance, LDL was borderline high in the LA group compared with HA group which include some obese/overweight individuals. Moreover, a significant correlation between vigorous PA and HDL levels was observed ($r = .27, p < .05$). Furthermore, vigorous PA might enhance the utility of foods containing omega-3 as there was a moderately positive correlation between omega-3 levels...
and vigorous PA. These findings raise the alert for further investigation to clarify the association between vigorous PA and fatty acids.

Adiponectin and leptin have been shown to be affected by exercise (Kao et al., 2021). Although there was no significant difference in adiponectin levels between the HA and LA groups, the LA group had higher (but not significant) adiponectin levels than the HA group. However, long-term moderate-intensity exercise at 60% to 70% of \( \text{HR}_{\text{max}} \) for approximately 200 min/week can significantly increase adiponectin levels in patients with obesity \( (p < .01) \) but not in lean women (Kondo et al., 2006). Regardless of the PA status, the lean female participants \( (n = 17) \) in the present study had significantly higher adiponectin levels than the lean male participants \( (n = 12, p < .001) \). The effect of PA status is therefore not fully clarified, and further investigations are warranted to identify the effect of PA on adiponectin levels.

The LA group had significantly higher plasma leptin levels than the HA group \( (p < .01) \). Exercise intensity and duration might play a role in plasma leptin levels (Kao et al., 2021), and long-term exercise training has been shown to affect leptin levels regardless of weight reduction (Hickey et al., 1997). Similar to a previous study (Elias et al., 2000), the HA group in the present study performed more vigorous PA \( (p = .01) \), which might partly explain why the HA group had lower leptin levels than the LA group.

The HA group showed lower hsCRP levels \( (p < .05) \), a difference that might have been due to the larger number of O,O participants in the LA group \( (52\% \text{ in the HA group vs. } 23\% \text{ in the LA group}) \). A previous study found that CRP levels were significantly decreased during the recovery period (eighth week) following a high-intensity exercise program (Andersson et al., 2010). Results of the present study reported that vigorous PA might contribute to reduced CRP levels in HA group which is concurrent with a recent finding (Cerqueira et al., 2020).

Acute exercise has been found to affect plasma IL-6 levels (Ostrowski et al., 1998); however, other studies have found no significant differences in IL-6 levels before and after exercise (Polak et al., 2006). Plasma IL-6 levels were not significantly different between the LA and HA groups. The influence of PA status on IL-6 levels is still vague, and the effect of PA status seems to be confounded by other factors, such as exercise type, duration, and intensity, as well as by weight reduction (Cerqueira et al., 2020; Monzillo et al., 2003).

Similarily, in the present study, there were no statistically significant differences between the LA and HA groups in terms of TNF-\( \alpha \) levels. A moderate exercise program had no effect on circulating TNF-\( \alpha \) levels (Polak et al., 2006), whereas 12 weeks of high-intensity exercise significantly reduced inducible TNF-\( \alpha \) synthesis in whole blood in healthy young and sedentary adults (Andersson et al., 2010). Although the HA group spent more time doing vigorous and highly vigorous PA than the LA group, there was no statistically significant difference in TNF-\( \alpha \) levels between the groups. Thus, the effect of PA intensity on TNF-\( \alpha \) levels is possibly related to indirect mechanisms.

There were no significant differences between the LA and HA groups in terms of fasting insulin, glucose, or HOMA-IR levels in the present study. A previous study reported that PA status plays a role in reducing and regulating plasma leptin levels. PA is also a strong determinant of insulin sensitivity, with or without obesity (Dashki Khavidaki et al., 2018; Kelley & Goodpaster, 1999). Leptin has been found to act as an insulin sensitizer and might contribute to insulin resistance when leptin levels are constantly elevated (Franks et al., 2007).

**Conclusion**

Based on the results of the present study, participants in the O/O and LA groups had a higher risk marker of CVD and more likely to develop CVDs than those in the L and HA groups. Body composition and PA intensity play independent and integrated roles in most of the classical and some of the newer CMDRMs. Interestingly, vigorous activity may improve health-related blood lipids such as HDL, LDL, and ARA/EPA ratio. Regardless of body composition status, low active participants were more likely to have higher levels of leptin and hsCRP. Furthermore, higher PA levels, particularly vigorous PA, are positively associated with CMDRMs.

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