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ORIGINAL PAPER

Physical Activity is Associated with Metabolic Health in Men Living with HIV

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Abstract Metabolic health is a cause for concern among those living with HIV, especially those on antiretroviral therapy. Physical activity (PA) is known to benefit metabolic health, however, few studies have objectively measured PA or investigated the relationship between PA and metabolic health among those living with HIV. In this study, PA and indices of metabolic health among twenty men living with HIV and twenty age matched HIV-negative men were measured. PA was measured using Actigraph accelerometers. Components of the metabolic syndrome and insulin resistance were measured using routine laboratory methods. Men living with HIV were significantly more physically active than HIV-negative men, and were reaching public PA guidelines. Significant inverse correlations between moderate PA and both insulin resistance (ρ -0.847; $p < 0.001$) and triglycerides (ρ -0.575; $p = 0.013$) were seen in those living with HIV. Results of this study emphasize the importance of an active lifestyle for those living with HIV.

Resumen La salud metabólica es un motivo de preocupación para las personas que viven con el VIH, en concreto para las que siguen tratamiento antirretrovírico. Se ha demostrado que la actividad física (AF) es beneficiosa para la salud metabólica. No obstante, muy pocos estudios han medido de forma objetiva la AF o investigado la relación existente entre la AF y la salud metabólica en personas que viven con el VIH. En este estudio se han medido la AF y los índices de salud metabólica en veinte hombres que viven con el VIH y veinte hombres agrupados por edad no infectados por el VIH. Para la medición de la AF se utilizaron acelerómetros Actigraph. Los componentes del síndrome metabólico y la resistencia a la insulina se midieron mediante métodos de laboratorio habituales. Los hombres que viven con el VIH se mostraron mucho más activos físicamente que los hombres no infectados por el VIH y se aproximaron a las directrices públicas de AF. Se observaron correlaciones inversas significativas entre la AF moderada y la resistencia a la insulina (ρ -0.847; $p < 0.001$) y los triglicéridos (ρ -0.575; $p = 0.013$) en personas que viven con el VIH. Los resultados de este estudio hacen hincapié en la importancia de un estilo de vida activo para aquellos que viven con el VIH.

Keywords HIV · Physical activity · Metabolic syndrome · Sedentary behavior

Introduction

The post combination antiretroviral therapy (ART) era has seen a dramatic change in the lives and longevity of people living with HIV. HIV is no longer fatal and is now considered a chronic disease. As such, the medical needs of those living with HIV have changed. Chronic conditions such as cardiovascular disease are now among the most common causes of death for people living with HIV [1].The side effects of ART, which directly alter metabolic processes, contribute greatly to the acceleration of chronic disease processes in this population [2]. Common side

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effects of ART include hypertension, high triglycerides and cholesterol, impaired fasting glucose and lipodystrophy [3]. Effective treatment for the poor metabolic profile seen in those living with HIV has not yet been established. Despite the high prevalence of the metabolic syndrome in this population [4] there is a dearth of information on the effects of lifestyle factors such as physical activity (PA) on indices of metabolic health in people living with HIV.

Current PA guidelines recommend that all adults accumulate 30 min of moderate intensity PA on 5 or more days a week, or 150 min of moderate PA a week comprising bouts lasting at least 10 min [5]. The approximate equivalent in steps is 10,000 steps a day. PA is safe, [6] has known benefits for those living with HIV [6, 7], and is an independent predictor of the metabolic syndrome among people living with HIV [8]. Despite this, the average quantity (i.e. total time) and pattern (i.e. the breakdown of duration and intensity per activity bout) of PA among those living with HIV are unclear. In a systematic review Schuelter-Trevisol concluded that study methodologies and the definition of PA between studies differed too much to enable a pooled estimate describing PA patterns of people living with HIV [9]. Various self-report questionnaire methods have been used to assess PA among people living with HIV, however the measurement properties of PA questionnaires, including their validity, are poor [10] and have been shown to result in overestimation and underestimation in patient populations [11, 12], including those living with HIV [13]. Accelerometers are therefore generally considered a more valid method of measuring habitual PA. Few studies have used accelerometers to measure PA in people living with HIV [13–15] or compared PA to an HIV-negative control group [16–20]. One of the main benefits of PA for those living with HIV is the potential benefit on metabolic health.

The objectives of this study were to objectively measure the quantity of PA men living with HIV are engaging in, and to compare this to a population of age matched HIV-negative men and public PA recommendations. It was also an objective to investigate the association between indices of metabolic health and PA.

Methods

This study was approved by the Joint Research Ethics Committee of the Adelaide and Meath Hospital, incorporating the National Children's Hospital and St. James's Hospital, and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Participants living with HIV were recruited from an outpatient clinic at St. James's Hospital. The clinic in question is the largest, free STI, HIV and Infectious Disease service in Ireland and is located in Dublin, Ireland's capital city. Eligible candidates were contacted about the study by phone, those who expressed an interest were subsequently posted an information leaflet and informed consent form. Those who returned completed consent forms were contacted again by phone to arrange a time to meet with a member of the research team. Age-matched control subjects comprised a convenience sample recruited through the staff at St. James's Hospital and from the local community. Informed consent was obtained from all individual participants included in the study.

Height was measured to the nearest 0.1 cm with a Seca 220 stadiometer during inhalation wearing no shoes. Weight was determined to the nearest 0.1 kg on Seca scales, wearing no shoes. BMI was calculated as $kg.m^{-2}$. Venous blood samples were taken at a routine clinic visit within 12 weeks of physical activity data collection. Glucose, insulin resistance, total cholesterol, triglycerides, and both high and low density lipoprotein cholesterol (HDL and LDL) were measured by routine laboratory methods following an overnight fast of at least 8 h. The International Diabetes Federation consensus worldwide definition of the metabolic syndrome was used to categorise participants as having or not having the metabolic syndrome [21].

PA was measured using ActiGraph GT3X+ triaxial accelerometers (48 E. Chase Street, Pensacola, FL 32502). These triaxial accelerometers measure movement on three planes to give an accurate representation of the quantity and pattern of PA while worn. In line with current recommendations for accelerometer use for the measurement of habitual physical activity [22, 23] participants were asked to wear the accelerometer at the level of their right hip during waking hours for 7 consecutive days, and were required to remove it when swimming, showering or bathing. A day of accelerometer data was considered valid if the participant wore the device for at least 10 h on that day [22]. As the actigraph is designed to detect acceleration and is not waterproof, it is not capable of measuring all types of exercise (e.g. water-based sports and resistance training). Participants were therefore asked to detail physical activities carried out, as well as the time they put the device on in the morning and took it off at night, in a diary provided to them by the research team.

Upon returning the accelerometers, Actigraph files were downloaded to the Actilife v 6.9.2 software programmes as GT3x files containing the raw data. These files were then exported as AGD files. An epoc length of 60 s was used. Exercise bouts and cut points for light, moderate and vigorous activity were determined using the system software of Actigraph (Freedson method). During accelerometer activation, unique identifier codes were used. The same codes were used to identify activity diaries. Accelerometer

data analysis was therefore carried out without knowledge of which group each participant was in. Exercise not detected by the Actigraph such as that accumulated through resistance training or water-based sports were manually added to Actigraph PA data. The intensity of these activities were determined from the compendium of physical activities for adults [24].

All participants were measured in the same clinic using the same protocol. Statistical analysis was carried out using IBM SPSS Version 22 with $p < 0.05$ considered statistically significant. Data were checked for normality using the Kolmogorov–Smirnov Test. Where it was discovered that variables did not follow a normal distribution, non-parametric analysis was used. Differences between groups were analysed using t-tests or Mann–Whitney U tests where appropriate. Associations between variables were analysed using Spearman and Pearson correlations where appropriate. Factorial ANOVA was used to determine whether there was a significant difference in MVPA between group (HIV-positive and HIV-negative) and presence of the metabolic syndrome (present or absent).

Results

Twenty men living with HIV and twenty age-matched HIV-negative men were recruited and consented to take part in the study. Participants were self-reported as well as biologically male. Data from one accelerometer was invalid and could not be used. Two participants dropped out and did not complete the study. Thus analysis was carried out on 37 men (19 in the control group and 18 in the HIV positive group). Characteristics of each group are detailed in Table 1. By study design, the age of participants did not differ between groups ($p = 0.709$). Mean age of those with HIV was 46 (SD12) and mean age of those without HIV was 45 years (SD 11). There was no difference between groups in smoking status, pack years, alcohol consumption of family history of a cardiac event. In the HIV-negative group 11 men reported that they were current or past smokers whereas 10 men reported that they were current or past smokers in the HIV-positive group.

Those living with HIV accumulated an average of 33 min of PA daily in bouts of at least 10 min. This exceeds minimal daily PA recommendations. HIV-negative participants accumulated a daily average of 16 min PA a day in bouts of at least 10 min. When bout length was not taken into account those living with HIV were shown to achieve an average of 55 min engaging in moderate to vigorous intensity PA daily. This was significantly longer than the HIV-negative group (Table 1). When analysed individually, just over half of the control population (10 men) had achieved PA recommendations whereas 15 of those living with HIV reached the recommendations. Examination of the pattern of PA accrual revealed that the difference between groups was due to those living with HIV engaging in significantly more bouts of PA and bouts being longer in duration. Those living with HIV were accumulating an average daily step count that was slightly below the recommended 10,000 steps, which may be explained by some PA being accumulated through non-ambulatory methods.

There was no significant difference between groups in total cholesterol, triglycerides, HDL, LDL, or any other blood marker measured. Four people in each group (approximately 21%) were considered to have the metabolic syndrome [21].

Among those living with HIV, correlation analysis revealed a significant inverse relationship between total time spent in moderate intensity activity and both insulin resistance and triglycerides (ρ −0.847; $p < 0.001$ and ρ −0.575; $p = 0.013$ respectively). Total time spent in moderate to vigorous PA (MVPA) was also significantly correlated with both insulin resistance (ρ −0.785; $p < 0.001$) and triglycerides (ρ −0.484; $p = 0.042$). No significant correlations between the quantity or pattern of PA and indicators of metabolic health were seen in the HIV-negative group. No significant correlations were seen between other PA variables (light intensity PA, duration of bouts or frequency of bouts) with indices of metabolic health.

To determine whether activity levels differed between those with the metabolic syndrome and those without the metabolic syndrome factorial ANOVA was conducted with group (HIV-positive and HIV-negative) and presence of the metabolic syndrome (having the metabolic syndrome or not having the metabolic syndrome) as fixed factors and total minutes of MVPA as the dependent variable. Results revealed a significant difference between those with and without the metabolic syndrome $F(1,33) = 7.78$, $p = 0.009$, and a significant interaction between group and presence of metabolic syndrome $F(1,33) = 6.58$, $p = 0.015$. Those with the metabolic syndrome engaged in significantly less moderate to vigorous physical activity (23 min; SD 8) than those without the metabolic syndrome (49 min; SD 4). The mean difference between groups was 26 min with a standard error of 9 min. The group with the lowest levels of physical activity were those living with HIV who also had the metabolic syndrome (Fig. 1).

Discussion

This study described the quantity and pattern of PA among a small sample of men living with HIV and compared them with a control group of age-matched HIV-negative men.

Table 1 Participant characteristics, physical activity and venous blood results

N = 37 (19 HIV−, 18 HIV +)	HIV-negative		HIV-positive		Difference between groups
	Mean or median	SD	Mean or median	SD	
Height (cm)	178	7	178	7	$t(35) = 0.01$, $p = 0.99$
Weight (kg)	86.8	12.8	85.3	9.3	$t(35) = 0.41$, $p = 0.69$
BMI ($kg.m^{-2}$)	27	4	27	2.5	$t(35) = 0.43$, $p = 0.67$
Waist circumference (cm)	96	10	101	24	$t(35) = 0.84$, $p = 0.41$
Number of daily PA bouts	0.6	0.5	1.7	1.3	$t(35) = -3.63$, $p < 0.01$[a]
Time spent in PA bouts a day (min)	16	16	33	24	$t(35) = -2.54$, $p = 0.02$[a]
Number of daily sedentary bouts	15	6	14	4	$t(35) = 0.59$, $p = 0.56$
Time spent in sedentary bouts a day (min)	323	140	299	96	$t(35) = 0.61$, $p = 0.549$
Sedentary[b] (min)	526		490		$U = 141$, $p = 0.36$
Light PA (min a day)	230	87	248	91	$t(35) = -0.60$, $p = 0.55$
Moderate PA (min a day)	29	17	50	34	$t(35) = -2.45$, $p = 0.02$[a]
Vigorous PA[b] (min a day)	0.3		2		$U = 160$, $p = 0.75$
Total MVPA (min a day)	31	17	55	35	$t(35) = -2.57$, $p = 0.02$[a]
Steps a day	5946	2368	9016	4183	$t(35) = -2.77$, $p < 0.01$[a]
Systolic BP (mmHg)	126	12	124	10	$t(35) = 0.56$, $p = 0.58$
Diastolic BP (mmHg)	81	9	78	6	$t(35) = 1.18$, $p = 0.25$
Total cholesterol (mmol/L)	4.92	1.08	4.72	0.91	$t(35) = 0.60$, $p = 0.55$
LDL (mmol/L)	2.91	1.01	2.62	0.84	$t(35) = 0.94$, $p = 0.35$
HDL (mmol/L)	1.38	0.26	1.34	0.38	$t(35) = 0.37$, $p = 0.71$
Triglyceride[b] s (mmol/L)	1.30		1.21		$U = 152$, $p = 0.56$
Fasting glucose (mmol/L)	5.0	0.6	5.2	0.5	$t(35) = -1.14$, $p = 0.26$
Insulin resistance[b] (HOMA- IR)	1.35		1.40		$U = 145$, $p = 0.59$
Pack years[b]	0		0		$U = 167$, $p = 0.65$
Alcohol[b] (reported average units per week)	8		10		$U = 169$, $p = 0.74$

Note Results expressed in minutes are rounded to the nearest minute

[a] Indicates statistically significant difference between groups

[b] Indicates non-normally distributed data – median reported instead of mean and non-parametric tests performed

Min minutes

BP Blood Pressure

PA Physical activity

MVPA Moderate to Vigorous Physical Activity

LDL low density lipoprotein

HDL high density lipoprotein

Note that a bout of physical activity must last at least 10 consecutive minutes

Note that a sedentary bout must last at least 10 consecutive minutes

Significant differences were seen in both the quantity and pattern of PA acquired. Those living with HIV were engaging in significantly more moderate to vigorous PA than the HIV-negative group. Those living with HIV were acquiring more bouts of PA and engaging in longer bouts than the HIV-negative group. Previous studies comparing PA between those living with HIV and a control population have found those living with HIV to be less active [16, 19], or have found no difference between groups [20]. One study reported those living with HIV to be more active [18]. The discrepancy in results between the current study and those previously reported may be explained by differences in measurement methods and population characteristics. Previous studies comparing those living with HIV to a control populations used questionnaires to assess PA [16, 18–20].

Interestingly, there was no difference between groups in sedentary behaviour. The quantity of time spent being sedentary however, is a cause for concern. Sedentary behaviour has been shown to be an independent risk factor

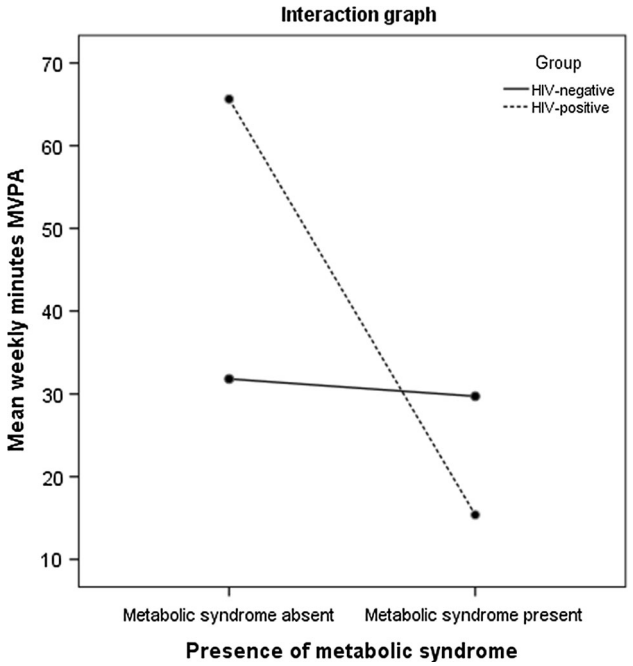

Fig. 1 Minutes of moderate to vigorous physical activity by group and presence of the metabolic syndrome. MVPA; moderate to vigorous physical activity

for certain chronic diseases including certain cancers, cardiovascular disease and the metabolic syndrome [25–28]. There are currently no specific recommendations for a safe length of time to be engaging in sedentary behaviour. However, interventions aimed at reducing sedentary behaviour may be of benefit to those living with HIV.

This study also showed that men living with HIV were achieving the quantity of PA recommended by general PA guidelines [5]. This is surprising since, worldwide, approximately 30% of adults are inactive [29] and rates of inactivity are even higher in patient populations. High levels of PA seen in this study could be attributed to patients' engagement with health care services which advocate chronic disease self-management strategies such as exercise. Recent years have seen an increase in efforts to keep those living with HIV engaged in medical care [30]. There is also a possibility of selection bias whereby active and engaged patients were more likely to volunteer to take part in this study, however the same selection bias could be argued for recruitment of the control group.

Although participants in this study living with HIV were significantly more physically active than the HIV-negative control group, the metabolic profile between groups was similar. Overall the metabolic profile of both groups, as well as the prevalence of the metabolic syndrome, was similar to that reported in the wider Irish population [31]. PA is independently associated with the metabolic syndrome among men living with HIV [8]. Our analysis revealed an inverse association between moderate to vigorous PA and both insulin resistance and triglycerides in this population. Previous studies in this area have suggested an association between PA and both insulin resistance [32] and triglycerides [33] without data achieving statistical significance, or reported no associations between PA and metabolic variables or the metabolic syndrome [13, 33]. Jaggers et al. found a statistically significant decrease in the number of metabolic syndrome components with increasing PA [14], however in regression analysis waist circumference was the only component of the metabolic syndrome significantly predicted by moderate PA levels [14]. Unlike in previous studies, associations between PA and metabolic variables in the present study may have reached significance due to the relatively high quantity of PA those living with HIV were engaging in, and the measurement method used. Using an accelerometer to collect activity data likely increased the validity of the analysis since it is an objective measure sensitive to small differences in activity. Of the studies which have analysed the association between components of the metabolic syndrome and PA in men living with HIV, few have used an objective measure of PA [13, 14].

Results of this study could be interpreted to suggest that the intensity as well as the overall volume of PA accumulated contribute to metabolic health in men living with HIV. No significant associations were seen between metabolic variables and the number of bouts of activity, or time spent being sedentary. Although this study was cross sectional in nature and therefore we cannot determine causality, it is physiologically plausible that the PA levels of those living with HIV in this study offset some of the negative metabolic effects of their chronic condition. This would explain why the incidence of the metabolic syndrome among those living with HIV in this study was the same as that reported for the control group and the wider Irish population. Furthermore interventional studies have shown improvements in the metabolic profile of people living with HIV with exercise [34–36]. It would be expected however that levels of physical activity would correlate with indices of metabolic health in the control group as well as the HIV positive group. This was not the case and could be attributed to the narrower range of physical activity levels seen in the control group, or variables that were not assessed as part of this study such as diet or occupation.

Interestingly, factorial analysis conducted as part of this study revealed that being HIV-positive alone did not predict activity levels, but presence of the metabolic syndrome did. More pertinent perhaps was the significant interaction between the presence of HIV and presence of the metabolic syndrome; those with both diagnosis, who would arguably

benefit most from engaging in physical activity, were least active. This result highlights the burden of multi-morbidity, and raises the question of whether patients with dual diagnosis, such as being HIV positive and having the metabolic syndrome, should be targeted for interventions encouraging physical activity, or provided with additional supports to achieve physical activity goals.

Strengths and Limitations

A strength of this study is the use of accelerometers for the quantification of physical activity levels. Accelerometers are valid, reliable and enable researchers to gather detail regarding the intensity of activity which is difficult to ascertain from self-report measures. However this study also comes with limitations. Firstly, the control group chosen were a convenience sample who were age-matched to the HIV-positive group, however they were not matched for other variables known to effect physical activity and the metabolic syndrome such as occupation, diet socio-economic class. For this reason, the rate of the metabolic disease and physical activity levels were also compared to population norms. Furthermore, despite a lack of detailed matching there was no difference between groups in body mass, BMI, smoking status, pack years, or alcohol consumption. It can therefore be deduced that the groups were well matched with regards to risk factors for the metabolic syndrome. It could be argued that the patient group increased their activity due to the fact that they were wearing an accelerometer. To determine whether such performance bias was an issue, the first two days of accelerometer data were omitted and analysis was repeated. This did not significantly alter results, as such we are confident that data collected is a valid reflection of habitual physical activity.

Conclusion

The novelty of our findings is that the quantity and pattern of objectively measured PA among those living with HIV were compared with those of an age- and gender-matched control group. Results of this study showed that those living with HIV are achieving public PA recommendations and that their metabolic profile is similar to that reported in the wider Irish population [31]. As the prevalence of the metabolic syndrome among people on ART is known to be higher than that of the general population [4], it is possible that the quantity of PA seen in the current study among those living with HIV is protective against the negative metabolic effects of ART. As this study was cross sectional, direct causation cannot be assumed, however results are encouraging for those living with HIV and highlight the importance of an active lifestyle.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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