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Inverse Relationship Between Physical Activity, Adiposity and Arterial Stiffness in Healthy Middle-aged Subjects

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9 4 healthy middle-aged subjects

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3 23 **Abstract**
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6 25 **Background:** Several obesity related factors are reported to exacerbate premature
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8 26 arterial stiffening, including inactivity and metabolic disarray. The aim of the present
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10 27 study was to investigate the relationship between physical activity, arterial stiffness
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12 28 and adiposity using objective methods. To further explore the role of adiposity in this
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14 29 complex process, obesity associated anthropometric and humoral biomarkers were
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16 30 measured.
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19 31 **Methods:** Seventy-nine healthy, lifelong non-smoking, subjects were recruited.
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21 32 Habitual physical activity was measured using accelerometry. Arterial stiffness
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23 33 (augmentation index; AIx & pulse wave velocity; PWV), was measured using
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25 34 tonometry. Body composition was estimated using bioimpedence. Adipose associated
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27 35 biomarkers, leptin and adiponectin, were also measured.
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29
30 36 **Results:** Sedentary time was significantly associated with AIx ($r=0.38$, $P<0.001$),
31
32 37 PWV ($r=0.33$, $P<0.01$), body fat composition ($r=0.40$, $P<0.001$) and age ($r=0.30$,
33
34 38 $P<0.01$). Moderate + vigorous activity was inversely correlated with AIx ($r= -0.28$,
35
36 39 $P<0.05$) body fat composition ($r=-0.30$, $P<0.01$), postprandial insulin ($r=-0.35$,
37
38 40 $P<0.01$) and leptin/adiponectin ratio ($r=-0.28$, $P<0.05$). Moderate + Vigorous activity,
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40 41 body fat composition and post prandial insulin remained independent predictors of
41
42 42 AIx but not PWV.
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44 43 **Conclusion:** The more time healthy individuals spend being sedentary, the greater
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46 44 their body fat and arterial stiffness. Conversely higher activity levels are associated
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48 45 with reduced body fat and less arterial stiffness.
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5 49 Arterial stiffening is an independent predictor of cardiovascular risk and target organ
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7 50 damage such as left ventricular hypertrophy, myocardial infarction, renal failure,
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9 51 retinopathy and vascular dementia.¹ Several factors, such as smoking, metabolic
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11 52 disease, adiposity and physical inactivity, are reported to accelerate vascular
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13 53 stiffening.^{2,3,4,5,6,7} Many of these factors are inter-related with inactivity predisposing
14
15 54 to adiposity, low-grade inflammation, metabolic disarray and arterial damage.^{3,7,8,9,10}
16
17 55 In contrast, when subjects spend more time being vigorously active during
18
19 56 adolescence they have less arterial stiffness in adulthood and the observed benefits are
20
21 57 related to changes in blood pressure, body composition, cardiorespiratory fitness and
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23 58 their metabolic profile.⁶ Consequently activity levels are considered of key
24
25 59 importance in maintaining metabolic and arterial health.

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29 60 However, many studies examining the impact of physical activity on arterial stiffness
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31 61 have used subjective questionnaires to quantify activity patterns with few studies
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33 62 adopting more objective methods such as accelerometry.^{2,3,5,6,10,11,12} In addition many
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35 63 of these studies have focused on subjects in different age/gender groups and in
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37 64 patients with established metabolic risk factors.^{10,11,13}

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41 65 Therefore, the aim of the present experiment was to simultaneously evaluate the
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43 66 association between activity levels and arterial wall changes in clinically healthy,
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45 67 middle-aged subjects, using objective methods. In order to further explore the
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47 68 complex relationship between physical activity, arterial wall properties and obesity,
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49 69 we investigated if the interrelationship of activity levels and arterial changes were
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51 70 correlated with adiposity associated anthropometric, metabolic, hormonal and
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53 71 inflammatory markers.

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73 Methods

74 Seventy-nine (51 male & 28 female) subjects were recruited from the general
75 population via poster advertisements in the local community within a 5 km radius of
76 the hospital where all the study protocols were performed. The study was approved by
77 Trinity College Dublin Ethics Committee. Written informed consent was obtained
78 from all subjects prior to testing protocols. Subjects were included if they were
79 lifelong never-smokers, free from cardiovascular disease, normotensive (<140/90
80 mmHg), had normal lipid profile (LDLc <4.0 mmol.L⁻¹), normal oral glucose
81 tolerance test responses (fasting & post prandial glucose <7 & <11 mmol.L⁻¹) and
82 moderate alcohol intake (male <21 units per week; female <14 units per week).
83 Subjects were excluded if they were receiving treatment for or had a history of
84 hypertension, hyperlipidaemia, diabetes or were taking any medications that affected
85 haemodynamic and/or metabolic responses.

86 Following a 12-hour overnight fast, enrolled subjects attended the Cardiovascular
87 Research Unit at Tallaght hospital. Various anthropometrical measurements were
88 recorded, including height (Seca 202, SECA, UK), weight (Avery E101, Avery, UK)
89 and waist circumference (Creative Health Products, USA). Body fat composition was
90 estimated using whole-body bioimpedance (TBF 410 GS, Tanita, UK).

91
92 Subjects completed a 2-hour oral glucose tolerance test (OGTT). Blood glucose and
93 insulin values were measured from venous blood samples before and after a 75g oral
94 glucose challenge. Homeostasis model assessment (HOMA), a measure of glycaemic
95 homeostasis, was calculated from fasting glucose and fasting insulin values (fasting
96 glucose × fasting insulin / 22.1). In addition, for each subject, glycosylated
97 haemoglobin (HbA_{1c}), full fasting lipid profile and the adipose associated blood

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3 98 markers, adiponectin and leptin were measured. Nonspecific markers of systemic
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5 99 inflammation such as white cell count (WCC) and high sensitivity c-reactive protein
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7 100 (hsCRP) were also measured to determine the potential impact of adipose associated
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9 101 inflammation.
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103 *Pulse wave analysis*

104 The aortic augmentation index (AIx), a measure of wave reflection and surrogate
105 marker of arterial stiffness, was calculated from pressure waveform measurements
106 recorded from the radial artery using a previously validated method (Sphygmacor,
107 AtCor Medical, Australia).^{4,14} Central aortic systolic and diastolic blood pressure was
108 calculated from the radial artery waveform using a previously validated transfer
109 function (Sphygmacor, AtCor Medical, Australia).¹⁴ The sphygmacor software
110 automatically generates an “operator index” as an indication of quality control. The
111 operator index is based on the pulse wave height/shape variation over ten successive
112 cardiac cycles. In the present experiment, the mean of three values with an operator
113 index $\geq 90\%$ were used.
114

115 *Pulse wave velocity*

116 Pulse wave velocity, a direct measure of carotid-femoral arterial stiffness, was
117 calculated from simultaneous recordings of the carotid and femoral pressure
118 waveform using a previously validated semi-automated method (Vicorder, Skidmore
119 Medical, U.K.).¹⁵ Briefly, two pressure sensitive transducer cuffs were fixed to the
120 subject’s neck and leg, recording the time delay (Td; ms⁻¹) between the carotid and
121 femoral pulse waveforms using the foot-to-foot method.¹⁵ The distance between the

Physical activity and arterial stiffness

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3 122 two sites was measured using a tape-measure (Dist; m). PWV was calculated by the
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5 123 “in-built” software (Td/Dist; m.s⁻¹).¹⁴
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10 125 *Physical activity*

11 126 A triaxial accelerometer (RT3, Stayhealthy, USA) was used to record routine daily
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13 127 physical patterns. The accelerometer records activity counts as mean acceleration
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15 128 (m.s⁻²) in the vertical (*x*), anteroposterior (*y*) and mediolateral (*z*) planes. The activity
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17 129 counts are then summarized as vector magnitude ($VM=[x^2 + y^2 + z^2]^{0.5}$).¹⁶ Physical
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19 130 activity data was recorded at 1 min intervals over seven consecutive days. A day was
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21 131 defined as the period where 70% of the subjects had recorded accelerometer data and
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23 132 80% of that period constituted a minimal day for inclusion in the data analysis.¹⁷ Data
24
25 133 from five consecutive days, including one weekend day (Tuesday-Saturday or
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27 134 Sunday-Thursday), were used to calculate the absolute and relative time spent being
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29 135 sedentary and participating in light, moderate and vigorous activity.^{18,19}
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36 137 *Statistics*

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38 138 Pearson’s Univariate correlation and Spearman’s Univariate correlation was used to
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40 139 examine the relationship between parametric and non-parametric data. Stepwise
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42 140 multiple regression was used to assess the relative contribution of chosen variables
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44 141 and arterial stiffness. An unpaired student’s t-test was used to detect differences
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46 142 between groups for normally distributed data and Wilcoxon’s test for non-normally
47
48 143 distributed data. Data are presented as mean±SD unless otherwise stated. (JMP
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50 144 Version 4.0, SAS Institute Inc, NC, USA).
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56 146 **Results**
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3 147 The physical, metabolic, haemodynamic characteristics and gender comparisons are
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5 148 outlined in Table 1. Similar to Irish general population averages, 53% of the group
6
7 149 had normal BMI, 38% were overweight and the remaining 9% were obese.²⁰ In
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9 150 addition, 48% of the group had a waist/height ratio >0.5 and had high body fat
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11 151 composition with respect to their age and gender. Gender comparisons revealed that
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13 152 Augmentation index was markedly higher in females compared to males, yet no
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15 153 differences in PWV, central BP or brachial BP were observed.
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20 155 All subjects had normal lipid profile, normal glycaemic profile and normal OGTT
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22 156 responses. All subjects had normal 24-hour ambulatory blood pressure responses (Sys
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24 157 <135/Dia <85 mmHg) and normal arterial stiffness with respect to age and gender.^{21,22}
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26 158 The non-specific markers of systemic inflammation, hsCRP and WCC, were also
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28 159 within normal ranges.
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32 161 Age was strongly correlated with both AIx ($r=0.52$; $P<0.0001$) and PWV ($r=0.49$;
33
34 162 $P<0.0001$). In addition, body fat composition was strongly correlated with AIx
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36 163 ($r=0.55$; $P<0.0001$) and 24-hour ambulatory diastolic blood pressure was associated
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38 164 with PWV ($r=0.25$; $P<0.05$).
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43 166 Mean daily wearing (on) duration of the accelerometer was 701 ± 91 min and mean
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45 167 daily “non-wearing” (off) duration was 728 ± 90 min (Figure 1a). Absolute and relative
46
47 168 time spent within activity thresholds can be seen in Figure 1b. Subjects spent 240 ± 63
48
49 169 min ($16.71\pm 4.44\%$) being sedentary and 448 ± 90 min ($31.06\pm 6.21\%$), 13 ± 14 min
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51 170 ($1.45\pm 2.23\%$) & 4 ± 8 min ($0.19\pm 0.35\%$) participating in Light, Moderate & Vigorous
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53 171 activities.
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Physical activity and arterial stiffness

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173 The results of the univariate correlation between the relative time spent in the four
174 activity zones (Sed, Light, Mod & Vig) and physical measures of obesity, arterial
175 stiffness, blood pressure, metabolic and adipose related humoral markers can be seen
176 in Table 2. Time spent being sedentary was significantly associated with age, body fat
177 composition, AIx and PWV. There was a significant inverse correlation between time-
178 spent being moderately active and body fat composition and fasting insulin.

179 Subjects spent little time participating in moderate activity and 28 subjects did not
180 spend any time participating in vigorous activity. In an attempt to overcome this
181 limitation, moderate and vigorous activity time was amalgamated (Mod+Vig) in a
182 univariate analysis. Mod+Vig activity was inversely correlated with body fat
183 composition ($r=-0.30$, $P<0.01$), postprandial insulin ($r=-0.35$, $P<0.01$),
184 leptin/adiponectin ratio ($r=-0.28$, $P<0.05$) and AIx ($r=-0.28$, $P<0.05$).

185 In order to identify the relative contribution of associated variables on arterial
186 stiffness, age, gender, body fat composition, heart rate, mean arterial pressure and
187 physical activity were included in two separate stepwise regression models to predict
188 AIx and PWV. Age, gender, body fat composition and heart rate remained significant
189 ($P<0.05$) correlates of AIx for all activity zones. The combined Mod+Vig activity, but
190 not individual Sed, Light, Mod and Vig activity zones, also remained as an
191 independent predictor of AIx ($P<0.05$). However, age remained the only significant
192 ($P<0.0001$) predictor of PWV.

193 To further identify the metabolic/hormonal consequences of physical inactivity and
194 premature arterial stiffening, age, body fat composition, leptin/adiponectin ratio,
195 postprandial insulin and arterial stiffness indices were included in separate regression
196 models. Body fat composition and postprandial insulin remained independent

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3 197 predictors of AIx. Again, age remained the only significant ($P<0.0001$) predictor of
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5 198 PWV.

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10 **Discussion**

11 201 The main findings of the study were that subjects who spend more time being
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13 202 sedentary have stiffer arteries and more body fat. Conversely, subjects that spend
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15 203 more time being active have less arterial stiffness and lower body fat. Unsurprisingly,
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17 204 in this healthy population, age remained the strongest predictor of arterial stiffness.
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19 205 However, body fat composition and postprandial insulin remained independent
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21 206 predictors of AIx indicating the presence of a disease continuum whereby physical
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23 207 inactivity and adiposity augment early vascular changes.
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29 209 Our findings are similar with previous studies using objective methods to quantify
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31 210 daily physical activity.^{3,10,11} Previous studies report that carotid β -stiffness in
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33 211 postmenopausal women is inversely correlated with time spent participating in low
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35 212 intensity (<4 MET) physical activity.²³ In addition, further studies report that older
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37 213 subjects, especially those with low cardiorespiratory fitness, that spend more time
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39 214 being lightly active (<3 METs) have less arterial stiffness, lower body fat, lower
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41 215 blood pressure and lower fasting glucose.²⁴ More recent research reports that physical
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43 216 activity is an independent predictor of arterial stiffness in hypertensive adults with
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45 217 varying degrees of metabolic disarray.¹⁰

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49 219 In the present study, females had significantly higher AIx compared to males despite
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52 220 no differences in age, heart rate and PWV were observed. Gender differences in AIx
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54 221 are mainly attributable to differences in height. In shorter individuals, the pulse wave
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Physical activity and arterial stiffness

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3 222 path length is smaller, and so, reflected waves coalesce with incident waves at an
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5 223 earlier time point during systole resulting in greater AIx.²⁵ These gender differences
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7 224 are not observed for PWV because it is calculated relative to distance (m.s⁻¹).
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11 226 The link between physical activity and arterial stiffness is complex. Physical activity
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13 227 can benefit arterial stiffness via its direct effects on the vasculature or indirectly via
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15 228 exercise induced changes in body composition and associated changes in metabolic
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17 229 and cardiovascular risk factors.
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23 231 Physical activity and exercise can directly benefit arterial stiffness and prevent
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25 232 premature arterial ageing via its effect on blood pressure and heart rate.^{26,27} Blood
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27 233 pressure is one of the major determinants of arterial stiffness. Exercise induced
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29 234 changes in microvascular structure and function can directly affect systolic and
30
31 235 diastolic blood pressure, thereby improving arterial stiffness.^{28,29} Increased heart rate
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33 236 negatively affects arterial stiffness via the viscoelastic effects of heart rate on the
34
35 237 arterial wall.³⁰ Increased heart rate is also associated with increased sympathetic
36
37 238 outflow, which is known to stiffen large and medium sized vessels.³¹ In the present
38
39 239 study, no significant association was observed between 24-hour ambulatory or central
40
41 240 aortic blood pressure and physical activity and no association was observed between
42
43 241 physical activity and heart rate. These data suggest that the relationship between
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45 242 physical activity, or lack thereof, and arterial stiffness was not mediated by the direct
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47 243 effect of activity on the vasculature.
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3 245 Physical activity can also indirectly impact arterial stiffness via its affect on body
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5 246 composition and subsequent alteration in adipose related inflammatory, metabolic and
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7 247 hormonal factors.⁶
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11 249 Obesity and adipose tissue distribution, specifically increased central/abdominal
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13 250 visceral adipose tissue, is strongly correlated with increased arterial stiffness.^{8,4,32}
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16 251 Activity induced changes in body fat composition can benefit arterial stiffness via
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18 252 modification of inflammatory, metabolic and adipose related humoral factors.^{6,13,33}
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23 254 Non-specific systemic inflammatory markers, such as hsCRP and WCC, and adipose
24
25 255 associated inflammatory markers, such as interleukin-6 (IL6), tumour necrosis factor
26
27 256 alpha (TNF α) and monocyte chemoattractant protein 1 (MCP-1), are associated with
28
29 257 increased adiposity, premature vascular ageing and arterial stiffness.^{5,9,34} In the
30
31 258 present study, although the adipocytokines were not measured, hsCRP and WCC were
32
33 259 clinically normal and not associated with any of the activity parameters or indices of
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35 260 arterial stiffness. These results suggest that abnormal immune responses were
36
37 261 probably not related to the activity related changes in arterial stiffness.
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43 263 In the present study, all subjects had normal OGTT responses yet postprandial insulin
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45 264 was inversely associated with time spent being moderately & vigorously active and
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47 265 independently associated with arterial stiffness. These results suggest that the
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49 266 relationship between physical activity, arterial stiffness and adiposity may be
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51 267 mediated via the deleterious affects of adiposity on endocrine function and glycaemic
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53 268 homeostasis. In support of this, previous studies have consistently reported the
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Physical activity and arterial stiffness

269 relationship between abdominal/visceral adiposity, metabolic disorder and arterial
270 stiffness in both healthy and diseased populations.^{35,36}

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272 Leptin/adiponectin ratio was associated with time spent being sedentary and moderate
273 & vigorous activity. The link between adiposity, leptin, adiponectin, metabolic
274 disarray and cardiovascular disease has been consistently reported.^{37,38} Furthermore, it
275 is suggested that hypertrophy of adipocytes, especially those at key anatomic
276 locations, results in abnormal paracrine function, disrupting vascular and metabolic
277 homeostasis.^{39,40,41}

278

279 In summary, the major findings of the present study were that time spent being
280 sedentary and time spent participating in moderate and vigorous activity was
281 associated with increased and decreased arterial stiffness and body fat. This is the first
282 study demonstrate the relationship between habitual physical activity and arterial wall
283 changes in healthy, middle-aged, life-long non-smoking subjects. Furthermore, the
284 results also indicate that adiposity and hyperinsulinaemia may be responsible for the
285 increased arterial stiffness in less active subjects. Future studies are needed to explore
286 the protective effect of physical activity and premature arterial stiffening or whether
287 weight loss alone is sufficient to actuate beneficial changes.

288

289 A major strength of the present study was that objective methods were used to
290 quantify daily habitual physical activity patterns. However, arbitrary activity
291 thresholds were used to determine time spent being sedentary, lightly active,
292 moderately active and vigorously active. Therefore, the relative intensity of the
293 activity categories may have differed for the wide age range of subjects (range: 21-59

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3 294 years) that participated in the study. Further studies adopting accelerometry as a
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5 295 means to examine routine physical activity patterns should consider these factors.
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16 300 **References**

17 301
18 302 1. Nadar SK, Tayebjee MH, Messerli F, Lip GY. Target organ damage in
19
20 303 hypertension: pathophysiology and implications for drug therapy. *Curr Pharm*
21
22 304 *Des.* 2006;12(13):1581-92.
23
24
25 305

26
27 306 2. Boreham CA, Ferreira I, Twisk JW, et al. Cardiorespiratory fitness, physical
28
29 307 activity, and arterial stiffness: the Northern Ireland Young Hearts Project.
30
31 308 *Hypertension.* 2004;44(5):721-6.
32
33
34 309

35
36 310 3. Gando Y, Yamamoto K, Murakami H, et al. Longer time spent in light physical
37
38 311 activity is associated with reduced arterial stiffness in older adults. *Hypertension.*
39
40 312 2010;56(3):540-6.
41
42
43 313

44
45 314 4. Maher V, O'Dowd M, Carey M, et al. Association of central obesity with early
46
47 315 Carotid intima-media thickening is independent of that from other risk factors. *Int*
48
49 316 *J Obes (Lond).* 2009;33(1):136-43.
50
51
52 317

53
54 318 5. Mahmud A, Feely J. Arterial stiffness is related to systemic inflammation in
55
56 319 essential hypertension. *Hypertension.* 2005;46(5):1118-22.
57
58
59
60

Physical activity and arterial stiffness

1
2
3 320

4
5 321 6. van de Laar RJ, Ferreira I, van Mechelen W, Prins MH, Twisk JW, Stehouwer
6
7 322 CD. Lifetime vigorous but not light-to-moderate habitual physical activity impacts
8
9 323 favourably on carotid stiffness in young adults: the Amsterdam growth and health
10
11 324 longitudinal study. *Hypertension*. 2010;55(1):33-9.

12
13 325

14
15 326 7. Tomiyama H, Hirayama Y, Hashimoto H, et al. The effects of changes in the
16
17 327 metabolic syndrome detection status on arterial stiffening: a prospective study.
18
19 328 *Hypertens Res*. 2006;29(9):673-8.

20
21 329

22
23 330 8. Lo J, Dolan SE, Kanter JR, et al. Effects of obesity, body composition, and
24
25 331 adiponectin on carotid intima-media thickness in health women. *J Clin Endocrinol*
26
27 332 *Metab*. 2006;91(5):1677-1682.

28
29 333

30
31 334 9. McEniery CM, Wilkinson IB. Large artery stiffness and inflammation. *J Hum*
32
33 335 *Hypertens*. 2005;19(7):507-9.

34
35 336

36
37 337 10. O'Donovan C1, Lithander FE, Raftery T, Gormley J, Mahmud A, Hussey J.
38
39 338 Inverse relationship between physical activity and arterial stiffness in adults with
40
41 339 hypertension. *J Phys Act Health*. 2014;11(2):272-7.

42
43 340

44
45 341 11. Sugawara J, Otsuki T, Tanabe T, et al. Physical activity duration, intensity,
46
47 342 and arterial stiffening in postmenopausal women. *Am J Hypertens*.
48
49 343 2006;19(10):1032-6.

50
51 344

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2
3 345 12. van der Laar RJ, Ferreira I, van Mechelen W et al. Lifetime vigorous but not
4
5 346 light-to-moderate habitual physical activity impacts favourably on carotid stiffness
6
7 347 in young adults: the Amsterdam Growth and Health Longitudinal Study.
8
9 348 *Hypertension*. 2010;55:33-39.
10
11 349
12
13 350 13. Crespo CJ, Palmieri MR, Perdomo RP, et al. The relationship of physical
14
15 351 activity and body weight with all-cause mortality: results from the Puerto Rico
16
17 352 Heart Health Program. *Ann Epidemiol*. 2002;12(8):543-52.
18
19 353
20
21 354 14. Kelly R, Hayward C, Avolio A, O'Rourke M. Noninvasive determination of
22
23 355 age-related changes in the human arterial pulse. *Circulation*. 1989;80(6):1652-9.
24
25 356
26
27 357 15. Hickson SS, Butlin M, Broad J, Avolio AP, Wilkinson IB, McEniery CM.
28
29 358 Validity and repeatability of the Vicorder apparatus: a comparison with the
30
31 359 SphygmoCor device. *Hypertens Res*. 2009;32(12):1079-85.
32
33 360
34
35 361 16. Hale LA, Pal J, Becker I. Measuring free-living physical activity in adults with
36
37 362 and without neurologic dysfunction with a triaxial accelerometer. *Arch Phys Med*
38
39 363 *Rehabil*. 2008;89(9):1765-71.
40
41 364
42
43 365 17. Catellier DJ, Hannan PJ, Murray DM, et al. Imputation of missing data when
44
45 366 measuring physical activity by accelerometry. *Med Sci Sports Exerc*.
46
47 367 2005;37:S555-62.
48
49 368
50
51
52
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56
57
58
59
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Physical activity and arterial stiffness

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2
3 369 18. Rowlands AV, Thomas PW, Eston RG, Topping R. Validation of the RT3
4
5 370 triaxial accelerometer for the assessment of physical activity. *Med Sci Sports*
6
7 371 *Exerc.* 2004;36(3):518-24.
8
9 372
10
11 373 19. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity
12
13 374 assessments in field-based research. *Med Sci Sports Exerc.* 2005;37:S531-43.
14
15 375
16
17 376 20. Harrington, J., Perry, I., Lutomski, J., et al. SLÁN 2007: Survey of Lifestyle,
18
19 377 Attitudes and Nutrition in Ireland. Dietary Habits of the Irish Population,
20
21 378 Department of Health and Children. 2008.
22
23 379
24
25 380 21. Mattace-Raso F, Hofman A, Verwoert GC, et al. Determinants of pulse wave
26
27 381 velocity in healthy people and in the presence of cardiovascular risk factors:
28
29 382 'establishing normal and reference values'. Reference Values for Arterial Stiffness'
30
31 383 Collaboration. *Eur Heart J.* 2010;31(19):2338-50.
32
33 384
34
35 385 22. O'Brien E, Asmar R, Beilin L, et al. European Society of Hypertension
36
37 386 Working Group on Blood Pressure Monitoring. Practice guidelines of the
38
39 387 European Society of Hypertension for clinic, ambulatory and self blood pressure
40
41 388 measurement. *Hypertens.* 2005;23(4):697-701.
42
43 389
44
45 390 23. Sugawara J, Otsuki T, Tanabe T, et al. Physical activity duration, intensity,
46
47 391 and arterial stiffening in postmenopausal women. *Am J Hypertens.*
48
49 392 2006;19(10):1032-6.
50
51 393
52
53
54
55
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57
58
59
60

1
2
3 394 24. Gando Y1, Yamamoto K, Murakami H, et al. Longer time spent in light
4
5 395 physical activity is associated with reduced arterial stiffness in older adults.
6
7 396 *Hypertens*. 2010;56(3):540-6.

8
9
10 397

11 398 25. McGrath BP1, Liang YL, Kotsopoulos D, Cameron JD. Impact of physical
12
13 399 and physiological factors on arterial function. *Clin Exp Pharmacol Physiol*.
14
15 400 2001;28(12):1104-7.

16
17
18 401

19
20 402 26. Rueckert PA, Slane PR, Lillis DL, Hanson P. Hemodynamic patterns and
21
22 403 duration of post-dynamic exercise hypotension in hypertensive humans. *Med Sci*
23
24 404 *Sports Exerc*. 1996;28(1):24-32.

25
26
27 405

28
29 406 27. Wallace JP, Bogle PG, King BA, Krasnoff JB, Jastremski CA. The magnitude
30
31 407 and duration of ambulatory blood pressure reduction following acute exercise. *J*
32
33 408 *Hum Hypertens*. 1999;13(6):361-6.

34
35
36 409

37
38 410 28. Green DJ. Exercise training as vascular medicine: direct impacts on the
39
40 411 vasculature in humans. *Exerc Sport Sci Rev*. 2009;37(4):196-202.

41
42
43 412

44
45 413 29. Thijssen DH, Maiorana AJ, O'Driscoll G, Cable NT, Hopman MT, Green DJ.
46
47 414 Impact of inactivity and exercise on the vasculature in humans. *Eur J Appl*
48
49 415 *Physiol*. 2010;108(5):845-75.

50
51
52 416

Physical activity and arterial stiffness

- 1
2
3 417 30. Park BJ, Lee HR, Shim JY, Lee JH, Jung DH, Lee YJ. Association between
4
5 418 resting heart rate and arterial stiffness in Korean adults. *Arch Cardiovasc Dis.*
6
7 419 2010;103(4):246-52.
8
9 420
10
11 421 31. Swierblewska E, Hering D, Kara T, et al. An independent relationship between
12
13 422 muscle sympathetic nerve activity and pulse wave velocity in normal humans. *J*
14
15 423 *Hypertens.* 2010;28(5):979-84.
16
17 424
18
19
20 425 32. Sutton-Tyrrell K, Newman A, Simonsick EM, et al. Aortic stiffness is
21
22 426 associated with visceral adiposity in older adults enrolled in the study of health,
23
24 427 aging, and body composition. *Hypertension.* 2001;38(3):429-33.
25
26 428
27
28
29 429 33. Faeh D, Braun J, Tarnutzer S, Bopp M. Obesity but not overweight is
30
31 430 associated with increased mortality risk. *Eur J Epidemiol.* 2011;26(8):647-55.
32
33 431
34
35 432 34. Phillips AC, Jiang CQ, Thomas GN, et al. White blood cell subsets are
36
37 433 associated with carotid intima-media thickness and pulse wave velocity in an older
38
39 434 Chinese population: the Guangzhou Biobank Cohort Study. *J Hum Hypertens.*
40
41 435 2012;26(8):485-92.
42
43 436
44
45
46 437 35. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG.
47
48 438 Aortic pulse-wave velocity and its relationship to mortality in diabetes and
49
50 439 glucose intolerance: an integrated index of vascular function? *Circulation.*
51
52 440 2002;15:106(16):2085-90.
53
54 441
55
56
57
58
59
60

- 1
2
3 442 36. Webb DR, Khunti K, Silverman R, et al. Impact of metabolic indices on
4
5 443 central artery stiffness: independent association of insulin resistance and glucose
6
7 444 with aortic pulse wave velocity. *Diabetologia*. 2010;53(6):1190-8.
8
9 445
10
11 446 37. Hajer GR, van Haeften TW, Visseren FL. Adipose tissue dysfunction in
12
13 447 obesity, diabetes, and vascular diseases. *Eur Heart J*. 2008;29(24):2959-71.
14
15 448
16
17 449 38. Hsueh WA, Law R. The central role of fat and effect of peroxisome
18
19 450 proliferator-activated receptor-gamma on progression of insulin resistance and
20
21 451 cardiovascular disease. *Am J Cardiol*. 2003;18:92(4A):3J-9J.
22
23 452
24
25 453 39. Bays HE, González-Campoy JM, Bray GA, et al. Pathogenic potential of
26
27 454 adipose tissue and metabolic consequences of adipocyte hypertrophy and
28
29 455 increased visceral adiposity. *Expert Rev Cardiovasc Ther*. 2008;6(3):343-68.
30
31 456
32
33 457 40. Li FY, Cheng KK, Lam KS, Vanhoutte PM, Xu A. Cross-talk between
34
35 458 adipose tissue and vasculature: role of adiponectin. *Acta Physiol (Oxf)*.
36
37 459 2011;203(1):167-80.
38
39 460
40
41 461 41. O'Connell J, Lynch L, Cawood TJ, et al. The relationship of omental and
42
43 462 subcutaneous adipocyte size to metabolic disease in severe obesity. *PLoS One*.
44
45 463 2010;5(4):e9997.
46
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Physical, metabolic, endocrine, inflammatory and haemodynamic characteristics		
	Male	Female
n	n=51	n=28
Age (years)	38±9	40±9
Height (cm)	177.9±6.7	164.4±5.2
Body mass (kg)	83.1±13.9	64.5±6.8
BMI (kg.m ²)	26.2±3.7	23.9±2.9
Waist (cm)	91.9±11.8	78.3±6.6
Waist/Height	0.52±0.06	0.47±0.05
Body fat (%)	22.3±6.7	30.1±5.3
Total Cholesterol (mmol.L ⁻¹)	3.20±0.75	3.07±0.71
Triglyceride (mmol.L ⁻¹)	1.04±0.43	0.87±0.29
HDLc (mmol.L ⁻¹)	1.33±0.36	1.66±0.41***
LDLc (mmol.L ⁻¹)	2.72±0.68	2.67±0.67
Glucose fast (mmol.L ⁻¹)	5.17±0.39	4.91±0.45
Glucose PP (mmol.L ⁻¹)	4.77±1.01	4.92±1.20
Insulin Fast (mU.L ⁻¹)	7.56±2.82	7.37±3.55
Insulin PP (mU.L ⁻¹)	23.85±28.03	27.52±23.94
HbA _{1c} (%)	5.30±0.30	5.21±0.31
HOMA _{IR}	1.78±0.70	1.65±0.77
Leptin (pg.mL ⁻¹ .10 ⁻²)	118.61±113.40	137.88±78.03
Adiponectin (pg.mL ⁻¹ .10 ⁻²)	59.10±27.42	60.68±32.19
Lept/Adipo	2.99±4.97	2.77±1.88
hsCRP (mg.L ⁻¹)	2.5±2.89	1.30±1.62
WCC (10 ⁹ .L ⁻¹)	5.90±1.75	5.87±1.71
24h Brachial Sys BP (mmHg)	119±7	111±9
24h Brachial Dia BP (mmHg)	69±6	66±7
Aortic Sys BP (mmHg)	109±8	105±10
Aortic Dia BP (mmHg)	75±7	71±7
Heart rate (beats.min ⁻¹)	60±8	63±9
AIx (%)	9.90±11.90	21.75±10.67****
PWV (m.s ⁻¹)	6.88±0.91	6.89±0.98

466 Table 1. Physical characteristics and risk factors. Body mass index (BMI), waist
 467 height ratio (waist/height) high density lipoprotein cholesterol (HDLc), low density
 468 lipoprotein cholesterol (LDLc), postprandial glucose (Glucose PP), postprandial
 469 insulin (Insulin PP), glycosylated haemoglobin (HbA_{1c}), homeostasis model
 470 assessment of insulin resistance (HOMA_{IR}), high sensitivity c-reactive protein
 471 (hsCRP), white cell count (WCC), 24-hour ambulatory brachial systolic blood
 472 pressure (24h Brachial Sys BP), 24-hour ambulatory brachial diastolic blood pressure
 473 (24h Brachial Dia BP), aortic systolic blood pressure (Aortic Sys BP), aortic diastolic
 474 blood pressure (Aortic Dia BP), augmentation index (AIx), pulse wave velocity

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475 (PWV). ** P<0.01, *** P<0.001, **** P<0.0001 significantly different compared to
476 males.
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Univariate analysis of activity and physical, metabolic, endocrine, inflammatory and haemodynamic characteristics					
	Sed	Light	Mod	Vig	Mod+Vig
	r	r	r	r	r
Age	0.30**	-0.11	-0.03	-0.20	-0.13
Body mass	0.06	-0.06	0.06	-0.06	0.10
BMI	0.20	-0.07	-0.04	-0.18	-0.07
Waist	0.18	0.01	-0.08	-0.16	-0.06
W/Height	0.23	-0.01	-0.18	-0.20	-0.16
Body fat	0.40***	0.04	-0.25*	-0.21	-0.30*
Total Cholesterol	0.07	-0.05	0.08	-0.08	-0.14
Triglyceride	0.10	-0.01	-0.20	-0.10	-0.16
HDLc	-0.06	-0.10	0.10	0.02	0.03
LDLc	0.16	-0.03	0.04	-0.11	-0.14
Glucose Fast	0.18	0.01	0.00	0.08	0.01
Glucose Post	0.09	0.01	-0.13	0.06	-0.05
Insulin Fast	0.14	-0.13	-0.14	-0.13	-0.20
Insulin Post	0.19	0.02	-0.25*	-0.21	-0.35**
HbA1c	-0.06	0.18	0.11	-0.03	0.03
HOMA	0.18	-0.14	-0.15	-0.12	-0.20
Leptin	0.27	0.04	-0.17	-0.17	-0.25
Adiponectin	0.05	-0.23	0.16	0.10	0.07
Lept/Adipo	0.23	0.10	-0.26	-0.22	-0.28*
hsCRP	0.04	0.16	-0.10	0.06	-0.05
WCC	-0.05	-0.18	-0.09	0.03	-0.05
24 h Sys	-0.07	0.07	0.12	0.02	0.17
24 h Dia	0.14	-0.01	0.07	-0.14	0.01
Aortic Sys	0.18	0.01	0.01	0.02	0.07
Aortic Dia	0.10	0.00	0.07	0.12	0.13
Heart rate	0.02	0.02	-0.04	-0.13	-0.09
AIx	0.38***	-0.04	-0.17	-0.10	-0.28*
PWV	0.33**	-0.23	0.00	-0.18	-0.12

479 Table 2. Spearman's Univariate analysis of relative time spent being sedentary (Sed),
 480 lightly active (Light), moderately active (Mod), vigorously active (Vig), combined
 481 moderate & vigorous activity (Mod+Vig) and indices of obesity, humoral factors and
 482 arterial stiffness. * P<0.05, ** P<0.01, *** P<0.001.

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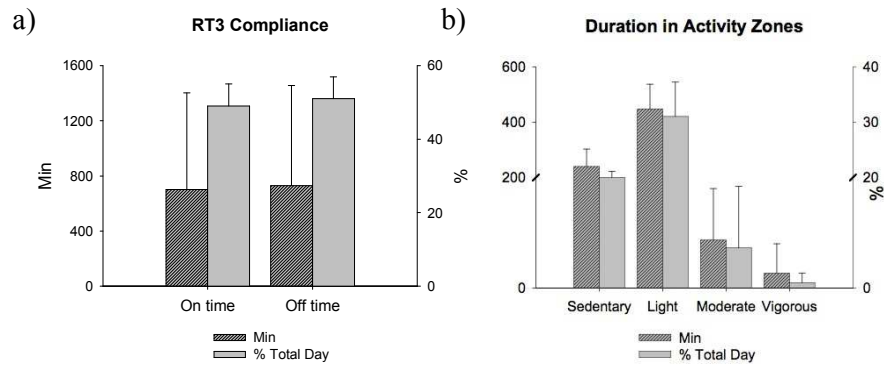
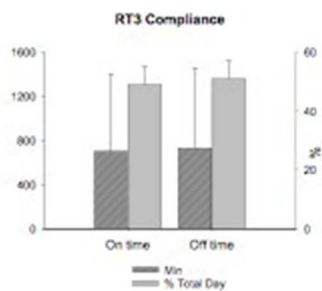


Figure 1. a) RT3 compliance. Absolute (min) and relative (%) time spent wearing (On time) and not wearing (Off time) the RT3. b) Absolute (Min) and relative (%) time spent within activity thresholds. Relative time is expressed as a percentage of an entire day (1440 min). Results are mean \pm SD.

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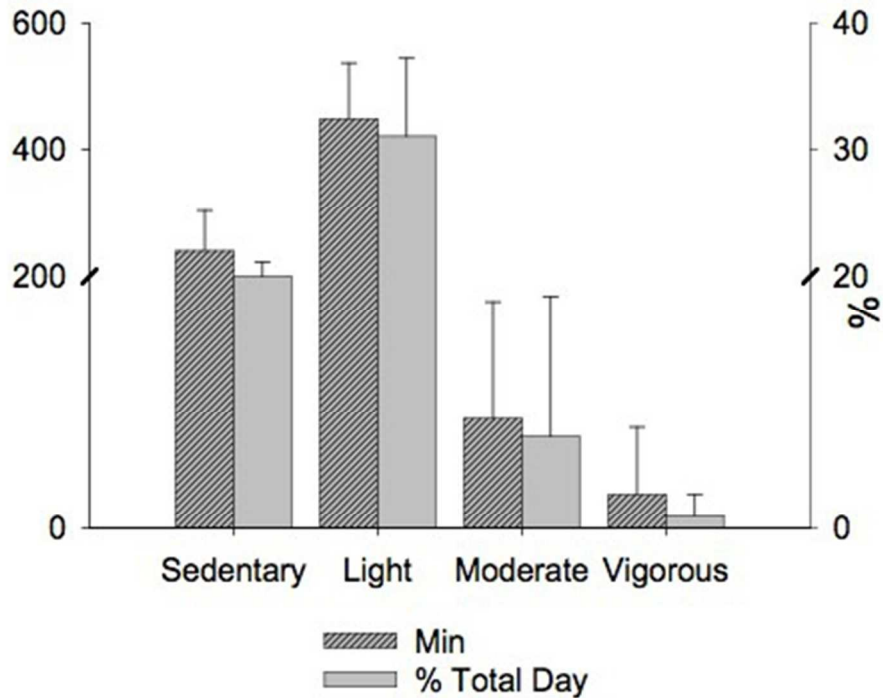


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Duration in Activity Zones



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view