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

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1 **Title page**

2 *1. Full title*

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Abstract

Background: Several obesity related factors are reported to exacerbate premature arterial stiffening, including inactivity and metabolic disarray. The aim of the present study was to investigate the relationship between physical activity, arterial stiffness and adiposity using objective methods. To further explore the role of adiposity in this complex process, obesity associated anthropometric and humoral biomarkers were measured.

Methods: Seventy-nine healthy, lifelong non-smoking, subjects were recruited. Habitual physical activity was measured using accelerometry. Arterial stiffness (augmentation index; AIx & pulse wave velocity; PWV), was measured using tonometry. Body composition was estimated using bioimpedence. Adipose associated biomarkers, leptin and adiponectin, were also measured.

Results: Sedentary time was significantly associated with AIx ($r=0.38$, $P<0.001$), PWV ($r=0.33$, $P<0.01$), body fat composition ($r=0.40$, $P<0.001$) and age ($r=0.30$, $P<0.01$). Moderate + vigorous activity was inversely correlated with AIx ($r=-0.28$, $P<0.05$) body fat composition ($r=-0.30$, $P<0.01$), postprandial insulin ($r=-0.35$, $P<0.01$) and leptin/adiponectin ratio ($r=-0.28$, $P<0.05$). Moderate + Vigorous activity, body fat composition and post prandial insulin remained independent predictors of AIx but not PWV.

Conclusion: The more time healthy individuals spend being sedentary, the greater their body fat and arterial stiffness. Conversely higher activity levels are associated with reduced body fat and less arterial stiffness.

48

49 Arterial stiffening is an independent predictor of cardiovascular risk and target organ

50 damage such as left ventricular hypertrophy, myocardial infarction, renal failure,

51 retinopathy and vascular dementia.¹ Several factors, such as smoking, metabolic

52 disease, adiposity and physical inactivity, are reported to accelerate vascular

53 stiffening.^{2,3,4,5,6,7} Many of these factors are inter-related with inactivity predisposing

54 to adiposity, low-grade inflammation, metabolic disarray and arterial damage.^{3,7,8,9,10}

55 In contrast, when subjects spend more time being vigorously active during

56 adolescence they have less arterial stiffness in adulthood and the observed benefits are

57 related to changes in blood pressure, body composition, cardiorespiratory fitness and

58 their metabolic profile.⁶ Consequently activity levels are considered of key

59 importance in maintaining metabolic and arterial health.

60 However, many studies examining the impact of physical activity on arterial stiffness

61 have used subjective questionnaires to quantify activity patterns with few studies

62 adopting more objective methods such as accelerometry.^{2,3,5,6,10,11,12} In addition many

63 of these studies have focused on subjects in different age/gender groups and in

64 patients with established metabolic risk factors.^{10,11,13}

65 Therefore, the aim of the present experiment was to simultaneously evaluate the

66 association between activity levels and arterial wall changes in clinically healthy,

67 middle-aged subjects, using objective methods. In order to further explore the

68 complex relationship between physical activity, arterial wall properties and obesity,

69 we investigated if the interrelationship of activity levels and arterial changes were

70 correlated with adiposity associated anthropometric, metabolic, hormonal and

71 inflammatory markers.

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 $\times$ fasting insulin / 22.1). In addition, for each subject, glycosylated
97 haemoglobin (HbA_{1c}), full fasting lipid profile and the adipose associated blood

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

102
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

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two sites was measured using a tape-measure (Dist; m). PWV was calculated by the “in-built” software ($Td/Dist; m.s^{-1}$).¹⁴

124

Physical activity

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

136

Statistics

Pearson’s Univariate correlation and Spearman’s Univariate correlation was used to examine the relationship between parametric and non-parametric data. Stepwise multiple regression was used to assess the relative contribution of chosen variables and arterial stiffness. An unpaired student’s t-test was used to detect differences between groups for normally distributed data and Wilcoxon’s test for non-normally distributed data. Data are presented as mean $\pm$ SD unless otherwise stated. (JMP Version 4.0, SAS Institute Inc, NC, USA).

145

Results

1
2
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
8
9 150 addition, 48% of the group had a waist/height ratio >0.5 and had high body fat
10
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
23
24 157 <135/Dia <85 mmHg) and normal arterial stiffness with respect to age and gender.^{21,22}
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27 158 The non-specific markers of systemic inflammation, hsCRP and WCC, were also
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29 159 within normal ranges.
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34 161 Age was strongly correlated with both AIx ($r=0.52$; $P<0.0001$) and PWV ($r=0.49$;
35
36 162 $P<0.0001$). In addition, body fat composition was strongly correlated with AIx
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38 163 ($r=0.55$; $P<0.0001$) and 24-hour ambulatory diastolic blood pressure was associated
39
40 164 with PWV ($r=0.25$; $P<0.05$).
41
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45 166 Mean daily wearing (on) duration of the accelerometer was 701 ± 91 min and mean
46
47 167 daily “non-wearing” (off) duration was 728 ± 90 min (Figure 1a). Absolute and relative
48
49 168 time spent within activity thresholds can be seen in Figure 1b. Subjects spent 240 ± 63
50
51 169 min ($16.71\pm4.44\%$) being sedentary and 448 ± 90 min ($31.06\pm6.21\%$), 13 ± 14 min
52
53 170 ($1.45\pm2.23\%$) & 4 ± 8 min ($0.19\pm0.35\%$) participating in Light, Moderate & Vigorous
54
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56 171 activities.
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Physical activity and arterial stiffness

172

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

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

200 **Discussion**

201 The main findings of the study were that subjects who spend more time being
202 sedentary have stiffer arteries and more body fat. Conversely, subjects that spend
203 more time being active have less arterial stiffness and lower body fat. Unsurprisingly,
204 in this healthy population, age remained the strongest predictor of arterial stiffness.
205 However, body fat composition and postprandial insulin remained independent
206 predictors of AIx indicating the presence of a disease continuum whereby physical
207 inactivity and adiposity augment early vascular changes.

209 Our findings are similar with previous studies using objective methods to quantify
210 daily physical activity.^{3,10,11} Previous studies report that carotid β -stiffness in
211 postmenopausal women is inversely correlated with time spent participating in low
212 intensity (<4 MET) physical activity.²³ In addition, further studies report that older
213 subjects, especially those with low cardiorespiratory fitness, that spend more time
214 being lightly active (<3 METs) have less arterial stiffness, lower body fat, lower
215 blood pressure and lower fasting glucose.²⁴ More recent research reports that physical
216 activity is an independent predictor of arterial stiffness in hypertensive adults with
217 varying degrees of metabolic disarray.¹⁰

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

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222 path length is smaller, and so, reflected waves coalesce with incident waves at an
223 earlier time point during systole resulting in greater AIx.²⁵ These gender differences
224 are not observed for PWV because it is calculated relative to distance (m.s⁻¹).

225

226 The link between physical activity and arterial stiffness is complex. Physical activity
227 can benefit arterial stiffness via its direct effects on the vasculature or indirectly via
228 exercise induced changes in body composition and associated changes in metabolic
229 and cardiovascular risk factors.

230

231 Physical activity and exercise can directly benefit arterial stiffness and prevent
232 premature arterial ageing via its effect on blood pressure and heart rate.^{26,27} Blood
233 pressure is one of the major determinants of arterial stiffness. Exercise induced
234 changes in microvascular structure and function can directly affect systolic and
235 diastolic blood pressure, thereby improving arterial stiffness.^{28,29} Increased heart rate
236 negatively affects arterial stiffness via the viscoelastic effects of heart rate on the
237 arterial wall.³⁰ Increased heart rate is also associated with increased sympathetic
238 outflow, which is known to stiffen large and medium sized vessels.³¹ In the present
239 study, no significant association was observed between 24-hour ambulatory or central
240 aortic blood pressure and physical activity and no association was observed between
241 physical activity and heart rate. These data suggest that the relationship between
242 physical activity, or lack thereof, and arterial stiffness was not mediated by the direct
243 effect of activity on the vasculature.

244

Physical activity can also indirectly impact arterial stiffness via its affect on body composition and subsequent alteration in adipose related inflammatory, metabolic and hormonal factors.⁶

Obesity and adipose tissue distribution, specifically increased central/abdominal visceral adipose tissue, is strongly correlated with increased arterial stiffness.^{8,4,32}

Activity induced changes in body fat composition can benefit arterial stiffness via modification of inflammatory, metabolic and adipose related humoral factors.^{6,13,33}

Non-specific systemic inflammatory markers, such as hsCRP and WCC, and adipose associated inflammatory markers, such as interleukin-6 (IL6), tumour necrosis factor alpha (TNF α) and monocyte chemoattractant protein 1 (MCP-1), are associated with increased adiposity, premature vascular ageing and arterial stiffness.^{5,9,34} In the present study, although the adipocytokines were not measured, hsCRP and WCC were clinically normal and not associated with any of the activity parameters or indices of arterial stiffness. These results suggest that abnormal immune responses were probably not related to the activity related changes in arterial stiffness.

In the present study, all subjects had normal OGTT responses yet postprandial insulin was inversely associated with time spent being moderately & vigorously active and independently associated with arterial stiffness. These results suggest that the relationship between physical activity, arterial stiffness and adiposity may be mediated via the deleterious affects of adiposity on endocrine function and glycaemic homeostasis. In support of this, previous studies have consistently reported the

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

271

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

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

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300 **References**

- 301
- 302 1. Nadar SK, Tayebjee MH, Messerli F, Lip GY. Target organ damage in
303 hypertension: pathophysiology and implications for drug therapy. *Curr Pharm*
304 *Des.* 2006;12(13):1581-92.
- 305
- 306 2. Boreham CA, Ferreira I, Twisk JW, et al. Cardiorespiratory fitness, physical
307 activity, and arterial stiffness: the Northern Ireland Young Hearts Project.
308 *Hypertension.* 2004;44(5):721-6.
- 309
- 310 3. Gando Y, Yamamoto K, Murakami H, et al. Longer time spent in light physical
311 activity is associated with reduced arterial stiffness in older adults. *Hypertension.*
312 2010;56(3):540-6.
- 313
- 314 4. Maher V, O'Dowd M, Carey M, et al. Association of central obesity with early
315 Carotid intima-media thickening is independent of that from other risk factors. *Int*
316 *J Obes (Lond).* 2009;33(1):136-43.
- 317
- 318 5. Mahmud A, Feely J. Arterial stiffness is related to systemic inflammation in
319 essential hypertension. *Hypertension.* 2005;46(5):1118-22.

Physical activity and arterial stiffness

320

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

325

7. Tomiyama H, Hirayama Y, Hashimoto H, et al. The effects of changes in the
metabolic syndrome detection status on arterial stiffening: a prospective study.
Hypertens Res. 2006;29(9):673-8.

329

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

333

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

336

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

340

11. Sugawara J, Otsuki T, Tanabe T, et al. Physical activity duration, intensity,
and arterial stiffening in postmenopausal women. *Am J Hypertens*.
2006;19(10):1032-6.

344

12. van der Laar RJ, Ferreira I, van Mechelen W et al. Lifetime vigorous but not light-to-moderate habitual physical activity impacts favourably on carotid stiffness in young adults: the Amsterdam Growth and Health Longitudinal Study. *Hypertension*. 2010;55:33-39.

13. Crespo CJ, Palmieri MR, Perdomo RP, et al. The relationship of physical activity and body weight with all-cause mortality: results from the Puerto Rico Heart Health Program. *Ann Epidemiol*. 2002;12(8):543-52.

14. Kelly R, Hayward C, Avolio A, O'Rourke M. Noninvasive determination of age-related changes in the human arterial pulse. *Circulation*. 1989;80(6):1652-9.

15. Hickson SS, Butlin M, Broad J, Avolio AP, Wilkinson IB, McEniery CM. Validity and repeatability of the Vicorder apparatus: a comparison with the SphygmoCor device. *Hypertens Res*. 2009;32(12):1079-85.

16. Hale LA, Pal J, Becker I. Measuring free-living physical activity in adults with and without neurologic dysfunction with a triaxial accelerometer. *Arch Phys Med Rehabil*. 2008;89(9):1765-71.

17. Catellier DJ, Hannan PJ, Murray DM, et al. Imputation of missing data when measuring physical activity by accelerometry. *Med Sci Sports Exerc*. 2005;37:S555-62.

Physical activity and arterial stiffness

18. Rowlands AV, Thomas PW, Eston RG, Topping R. Validation of the RT3 triaxial accelerometer for the assessment of physical activity. *Med Sci Sports Exerc.* 2004;36(3):518-24.
19. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc.* 2005;37:S531-43.
20. Harrington, J., Perry, I., Lutonski, J., et al. SLÁN 2007: Survey of Lifestyle, Attitudes and Nutrition in Ireland. Dietary Habits of the Irish Population, Department of Health and Children. 2008.
21. Mattace-Raso F, Hofman A, Verwoert GC, et al. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values'. Reference Values for Arterial Stiffness' Collaboration. *Eur Heart J.* 2010;31(19):2338-50.
22. O'Brien E, Asmar R, Beilin L, et al. European Society of Hypertension Working Group on Blood Pressure Monitoring. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. *Hypertens.* 2005;23(4):697-701.
23. Sugawara J, Otsuki T, Tanabe T, et al. Physical activity duration, intensity, and arterial stiffening in postmenopausal women. *Am J Hypertens.* 2006;19(10):1032-6.

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

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

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

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

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

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

Physical activity and arterial stiffness

30. Park BJ, Lee HR, Shim JY, Lee JH, Jung DH, Lee YJ. Association between resting heart rate and arterial stiffness in Korean adults. *Arch Cardiovasc Dis*. 2010;103(4):246-52.
31. Swierblewska E, Hering D, Kara T, et al. An independent relationship between muscle sympathetic nerve activity and pulse wave velocity in normal humans. *J Hypertens*. 2010;28(5):979-84.
32. Sutton-Tyrrell K, Newman A, Simonsick EM, et al. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. *Hypertension*. 2001;38(3):429-33.
33. Faeh D, Braun J, Tarnutzer S, Bopp M. Obesity but not overweight is associated with increased mortality risk. *Eur J Epidemiol*. 2011;26(8):647-55.
34. Phillips AC, Jiang CQ, Thomas GN, et al. White blood cell subsets are associated with carotid intima-media thickness and pulse wave velocity in an older Chinese population: the Guangzhou Biobank Cohort Study. *J Hum Hypertens*. 2012;26(8):485-92.
35. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? *Circulation*. 2002;106(16):2085-90.

36. Webb DR, Khunti K, Silverman R, et al. Impact of metabolic indices on central artery stiffness: independent association of insulin resistance and glucose with aortic pulse wave velocity. *Diabetologia*. 2010;53(6):1190-8.

37. Hajer GR, van Haeften TW, Visseren FL. Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. *Eur Heart J*. 2008;29(24):2959-71.

38. Hsueh WA, Law R. The central role of fat and effect of peroxisome proliferator-activated receptor-gamma on progression of insulin resistance and cardiovascular disease. *Am J Cardiol*. 2003;18:92(4A):3J-9J.

39. Bays HE, González-Campoy JM, Bray GA, et al. Pathogenic potential of adipose tissue and metabolic consequences of adipocyte hypertrophy and increased visceral adiposity. *Expert Rev Cardiovasc Ther*. 2008;6(3):343-68.

40. Li FY, Cheng KK, Lam KS, Vanhoutte PM, Xu A. Cross-talk between adipose tissue and vasculature: role of adiponectin. *Acta Physiol (Oxf)*. 2011;203(1):167-80.

41. O'Connell J, Lynch L, Cawood TJ, et al. The relationship of omental and subcutaneous adipocyte size to metabolic disease in severe obesity. *PLoS One*. 2010;5(4):e9997.

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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

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

(PWV). ** P<0.01, *** P<0.001, **** P<0.0001 significantly different compared to males.

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Univariate analysis of activity and physical, metabolic, endocrine, inflammatory and haemodynamic characteristics					
	Sed r	Light r	Mod r	Vig r	Mod+Vig 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

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

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±SD.

62x50mm (72 x 72 DPI)

Duration in Activity Zones

174x143mm (72 x 72 DPI)