Title: Objectively-measured sedentary time and its association with markers of cardiometabolic health and fitness among cardiac rehabilitation graduates

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ABSTRACT

Background: Sedentary time is an independent risk factor for cardiometabolic disease and mortality. It is unknown how much time individuals with coronary artery disease spend being sedentary or how their sedentary time relates to markers of health. The objectives of this study were to: (1) quantify sedentary time in a post-cardiac rehabilitation (CR) population, and (2) assess association with cardiometabolic risk, independent of moderate-to-vigorous physical activity (MVPA).

Design: Cross-sectional

Methods: As part of a larger trial, 263 recent CR graduates (~10 days post- cardiac rehabilitation, mean age=63.6±9.3 years, 75% male) wore an ActiGraph GT3X accelerometer during waking hours (≥4 days, ≥10 hours/day) to quantify sedentary time (≤150 counts-per-minute). Spearman correlations were computed to assess relationships between sedentary time (adjusted for wear time) with markers of cardiometabolic health and fitness. Significant markers were examined using multiple linear regressions.

Results: Participants spent an average of almost 8 hours/day sedentary (~14 bouts/day). Sedentary time was negatively correlated with high-density lipoprotein and $\dot{V}O_2$peak and positively correlated with triglycerides, body mass index (BMI) and waist circumference. After adjusting for age, sex, medications and MVPA, hours/day of sedentary time remained significantly associated with log$\dot{V}O_2$peak (β=-0.02, p=0.003) and BMI (β=0.47, p=0.03).

Conclusions: Findings suggest that even among a group of post-CR individuals who are already likely more active than patients who have not undergone CR, sedentary time remains high and is associated with poorer cardiorespiratory fitness, suggesting a possible new area of focus among CR programs.

Keywords: Sedentary Lifestyle; Motor Activity; Heart Diseases; Rehabilitation

INTRODUCTION

The majority of Canadian adults' waking time is spent being sedentary.[1] Sedentary behaviour refers to an energy expenditure ≤1.5 metabolic equivalents while in a sitting or reclining posture during waking hours and not simply the absence of physical activity.[2] Research consistently identifies sedentary behaviour as an independent risk factor for chronic diseases including cardiovascular disease, diabetes and cancer, as well as premature mortality.[3, 4]

Cardiovascular diseases, including coronary artery disease (CAD), are the leading cause of mortality globally.[5] Importantly, CAD outcomes are largely dependent on gains in cardiometabolic fitness achieved via exercise interventions (e.g. cardiac rehabilitation [CR]).[6, 7] Cardiac rehabilitation is an evidence-based, standard of care for those who have experienced an acute coronary syndrome, coronary revascularization and other cardiac conditions. It is recommended in CR that patients achieve 30-60 minutes of moderate-to-vigorous physical activity (MVPA) on most, preferably, all days of the week.[6] While the benefits of regular MVPA have been established, there has been little research examining to what extent sedentary time has an independent effect on cardiometabolic health and fitness in patients with CAD. Further, CR guidelines do not include any recommendations for sedentary time in patients with CAD, though they do recognize sedentary lifestyle (including sedentary time and physical inactivity) as a risk factor,[8] and research has shown that physical activity-focused programs/interventions are not likely to yield meaningful reductions in sedentary time.[9]

While there is limited data to suggest that individuals with cardiovascular disease have greater sedentary behaviour than those without[10], there is currently no published data to quantify

sedentary time in patients with CAD or how sedentary time relates to health outcomes in this population. Sedentary time is hypothesized to be greater in this population because it is both a risk factor for CAD and because it can lead to metabolic dysfunction and vascular damage.[11] In addition to the lack of descriptive data on sedentary time in this population, there is very limited research describing the relationship between sedentary time and cardiorespiratory fitness.[12]

Although CR guidelines promote that patients achieve 30-60 minutes of MVPA per day,[6] they may also need to consider evidence around sedentary time from general populations, as the lessons learned are likely to have a greater impact in a CAD population. Therefore, the objectives of this cross-sectional study were to: (1) quantify sedentary behaviours in a post-CR CAD population, and (2) assess associations between sedentary behaviours and measures of cardiometabolic health and fitness, independent of MVPA. The hypothesis of the study was that sedentary time would be related to markers of cardiometabolic health and fitness, with greater sedentary time being associated with poorer measures of health.

METHODS

This cross-sectional study was conducted at two sites: the University of Ottawa Heart Institute (UOHI) and University Health Network (UHN) in Ontario, Canada. Secondary analysis of data from cardiac patients enrolled in an ongoing randomized controlled trial (RCT) named ECologically Optimizing exercise maintenance in men and women Post-CR (ECO-PCR) was undertaken. The trial evaluates the efficacy of an exercise facilitator-led intervention on long-term exercise maintenance among patients who have completed CR in comparison to usual care. This research received ethical approval from the UOHI Human Research Ethics Board (UOHI #201200579-01) and the UHN Research Ethics Board (UHN 12-5018-AE9l).

Participants

Cardiac rehabilitation graduates from supervised programs were approached to participate. ECO-PCR inclusion and exclusion criteria have been described elsewhere (http://clinicaltrials.gov/ct2/show/NCT01658683). All participants had established CAD, with majority referred to CR following a percutaneous coronary intervention, coronary artery bypass graft surgery or myocardial infarction. A total of 1736 patients were screened for eligibility, 541 were deemed eligible and 300 were randomized to the RCT. Adults with complete baseline accelerometer data at the time of this sub-study were selected (N=278). All participants provided written informed consent prior to participating.

Procedures

Cardiac rehabilitation participants were approached at one of their last classes to solicit participation. Consenting participants were provided a self-report survey assessing sociodemographic characteristics. Clinical characteristics were extracted from charts, including indicators of cardiometabolic health and fitness from their CR discharge assessment.

Participants were asked to wear an ActiGraph GT3X accelerometer (ActiGraph, Pensacola, FL) on their right hip during waking hours for nine days. Participants were instructed to remove the monitor while sleeping or during water-related activities (e.g., swimming or bathing). The GT3X accelerometer is a lightweight and compact triaxial accelerometer that captures movement about the vertical (y-axis), horizontal (x-axis) and perpendicular (z-axis) axes. It also provides output for the vector magnitude; a composite measure of all three axes (vector magnitude = $\sqrt{(x^2 + y^2 + z^2)}$). A 15-second sampling epoch was used and converted into counts·min^{-1} (cpm).

Counts are a reflection of the frequency and intensity of the raw acceleration values and are summed based on epochs (i.e., 'chunks' of time).

Accelerometer data reduction

A valid day was defined as ≥10 hours of wear time, and participants were required to have a minimum of four valid to be retained in the analyses.[1] For participants with >7 valid days, the first day was removed (to minimize reactivity), and the subsequent seven days used for the average. Wear time was calculated by subtracting non-wear time from 24 hours. Non-wear time was defined as at least 60 minutes of consecutive zeros for counts, with an allowance of up to two minutes of counts between zero and 150.

Sedentary time was defined using a previously validated cut-point of ≤150 cpm for use with vector magnitude.[13] Sedentary bouts are defined as the number of bouts (≥10 consecutive minutes) of sedentary time detected per day. Each interruption in sedentary time (>150cpm) was considered a break. The data analysis used the '*ignore first sedentary break of each day*' to remove sedentary time accrued while the device was theoretically removed at night. If this was not removed the total time in sedentary breaks would be larger than the total wear time.

MVPA was defined using a cut-point of ≥2690 cpm for use with vector magnitude.[14] Minutes spent in bouts (≥10 consecutive minutes) were used to quantify MVPA.[15] Weekly averages were calculated by multiplying the daily average (minutes/day) by seven. Steps-per-day were also captured by the accelerometers.

Markers of cardiometabolic health

Baseline data were extracted from CR charts for several cardiometabolic markers of health, including: measured height and weight to determine body mass index (BMI) in kg/m^2, measured waist circumference, waist-to-height ratio, systolic and diastolic blood pressure (BP), HbA1c percentage, triglycerides, total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL).

Markers of cardiorespiratory fitness

After initial randomization to treatment group in ECO-PCR, participants were stratified by treatment group and randomly assigned to one of two exercise testing conditions: graded exercise tests required (50% of sample); or graded exercise tests not required (50% of sample). A symptom-limited graded exercise test with electrocardiographic monitoring using a ramp protocol on a treadmill to obtain $\dot{V}O_2peak$ ($mL \cdot kg \cdot min^{-1}$) as an indicator of cardiorespiratory fitness. Exercise tolerance was also assessed among all participants using the Duke Activity Status Index (DASI), a self-administered questionnaire that measures functional capacity.[16]

Statistical analysis

All analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Summary data were tested for normality using plots and Shapiro-Wilk's test statistics. Descriptive data were reported using means ± standard deviation or frequencies and percentages. Mean values between males and females were compared using the Wilcoxon-Mann-Whitney test. Spearman correlations were computed to assess relationships between wear time-adjusted sedentary time, bouts of sedentary time and breaks in sedentary time with markers of cardiometabolic health and fitness assessed at CR exit. Cardiometabolic markers that were significantly correlated with sedentary time were then examined using linear regression,

controlling for age, sex, medications, wear time and MVPA. All non-linear variables were log-transformed using base-10 logs prior to entry into the linear regression models.

Adjustments were made for age and sex as cardiorespiratory fitness levels are known to decline with age and are known to be more strongly linked with risk factors and cardiovascular disease among males than females.[17, 18] Moderate-to-vigorous physical activity was adjusted for wear time by using the residuals produced by regressing MVPA bout time on total wear time.[19]

RESULTS

Of the 278 trial participants, 263 (95%) with valid accelerometer results were used for the analyses. The majority (81%) had a minimum of seven valid days of data. Results were similar regardless of whether missing days were imputed based on daily averages or when only using those with seven days of valid data.

Table 1 provides participant characteristics. On average, participants were considered to be well-educated, married, non-smokers, overweight, normotensive, appeared to have well-managed lipids, and had a moderate-to-high functional capacity.[20, 21] Women were older, had greater total cholesterol, HDL and LDL and were more likely to be retired. Men had greater BMI, WC, DBP, DASI scores, and $\dot{V}O_2$peak values.

Movement patterns are described in Table 2. On average, participants spent almost 8 hours/day or 56% of their waking day being sedentary and only 3% of their day in bouts of MVPA. Sedentary time was accumulated in 14 bouts per day with an average of 13 breaks per day.

Males accumulated significantly more sedentary time than females (mean difference = 59.4 minutes/day).

Spearman correlations between sedentary time and the markers of cardiometabolic health and fitness identified significant positive correlations with BMI (r=0.16, p=0.009), waist circumference (r=0.17, p=0.007) and triglycerides (r=0.13, p=0.03) and significant negative correlations with HDL (r=-0.17, p=0.005) and $\dot{V}O_2$peak (r=-0.19, p=0.02). Correlations with sedentary bouts and sedentary breaks were similar for BMI (bouts: r=0.17, p=0.007; breaks: r=0.16, p=0.008) and waist circumference (r=0.16, p=0.01 for both), were lower for HDL (-0.14, p=0.02 for both) and not significant for triglycerides or $\dot{V}O_2$peak. Sedentary time was highly correlated with breaks (r=0.84) and bouts (r=0.83).

Average time in bouts, HDL, triglycerides, and $\dot{V}O_2$peak were not normally distributed and log-transformed prior to entry into the regression models. Results of the linear regression analyses (Table 3) identified that wear time-adjusted sedentary time was significantly associated with BMI, waist circumference, logHDL, and log$\dot{V}O_2$peak, but not log-triglycerides. For example, for every 1 hour increase of sedentary time per day, waist circumference increased by ~2 cm and $\dot{V}O_2$peak decreased by 1.05 mL/kg/min. Adjusting for MVPA did not change the strength of the associations. Adding age and sex to the models rendered waist circumference and logHDL no longer significant, but strengthened the association with log$\dot{V}O_2$peak; further adjusting for medication did not change the associations. Based on results from the correlation analysis, as well as the fully adjusted models, compared to the other outcomes assessed, sedentary time showed the strongest association with log$\dot{V}O_2$peak.

DISCUSSION

The results of the study indicate that even among a group of post-CR CAD patients, to whom active living has been promoted, the majority of waking time was spent engaged in sedentary behaviours. Further, the majority of these patients were not meeting MVPA guidelines.[6] Males were more sedentary than females. Sedentary time was negatively associated with $\dot{V}O_2$peak and positively associated with BMI independent of age, sex, wear time, medications and MVPA. Total sedentary time was more consistently associated with markers of cardiometabolic health and fitness than breaks in sedentary time and bouts of sedentary time.

The CR graduates in this study spent 56% of their waking day being sedentary, with much of this time spent in prolonged bouts. Evidence suggests that those participating in physical activity-focused interventions are not likely to reduce their sedentary time by a meaningful amount.[9] It is postulated that those who exercise may actually compensate for this good behavior by feeling less guilt for sitting once the exercise is complete. As this study is cross-sectional it is not possible to gauge if sedentary time was reduced as a result of CR. Future research is needed to compare sedentary behaviour in patients pre-CR and among those who have not participated in CR to ascertain whether CR participation is associated with lower sedentary behaviour. This may inform sedentary behaviour recommendations in CR, if evolving evidence continues to demonstrate that sedentary behaviour is independently associated with poorer health outcomes in cardiac and non-cardiac patients. Regardless, given the current state of the evidence around sedentary behaviour, replacing sedentary time with light or greater intensity movements has beneficial effects on health risk.[22]

Sex differences in activity patterns were observed. Male CAD patients spent a significantly greater proportion of their day engaged in sedentary behaviour (58% vs. 52%); while females spent a greater amount of time in light PA or incidental movement. This finding is consistent with population-level data showing that after the age of 60 the trend reverses with males being more sedentary.[23]

Similar to other studies, a gradient in association was observed between greater sedentary time and greater BMI and waist circumference and lower HDL and $\dot{V}O_2$peak.[12, 24-26] Interestingly, waist-to-height ratio which has been shown to be a better predictor of cardiovascular disease risk,[27] was not significantly associated with sedentary time. The ratio appears to remove issues associated with age and sex for measuring risk[27] and helps to explain how waist circumference is no longer significant after adjustment for age and sex. The lack of association between blood glucose control and sedentary time was consistent with previous studies.[19, 24] This lack of association is likely explained by the fact that associations are usually observed for insulin rather than glucose, which mechanistically has been shown to be more acutely affected by the lack of muscle contractility observed during bouts of sedentary time.[11]

Previous studies in apparently healthy populations have shown mixed findings with some showing significant associations[19, 28] and others showing no association[19, 24, 26] between sedentary time and total cholesterol, LDL, or BP. Sedentary time is likely related to these factors through similar pathways as exercise. Literature has consistently documented that exercise is related to HDL and triglyceride values, but not LDL.[29, 30] Further, the findings are also likely explained by the large number of participants taking statins, ACE-inhibitors and beta-blockers for lowering cholesterol (specifically LDL) and BP.[31, 32] The majority had well-controlled lipids and BP.

The strongest relationship was observed between sedentary time and $\dot{V}O_2$peak, independent of MVPA. This finding is of particular importance given the prognostic value of cardiorespiratory fitness on cardiovascular health and mortality,[33] especially among CR patients.[34] The findings herein are also consistent with previous studies showing negative associations between sedentary time and cardiorespiratory fitness in general population samples.[12, 25] Given that gains in cardiorespiratory fitness is one of the key indicators of CR success,[35] and that the present study identified a significant association between sedentary time and $\dot{V}O_2$peak in a post-CR CAD population, further longitudinal or interventional study investigations are warranted to establish the directional effects of sedentary time on cardiorespriatory fitness. Further, while MVPA and $\dot{V}O_2$peak were more strongly correlated (r=0.37), reducing sedentary time likely provides additional benefits and may be an easier target for patients.

This study is not without limitations. The greatest limitation is that this study was cross-sectional in design, and therefore no causal conclusions can be drawn. As such, the identification of directionality between sedentary time and the markers of cardiometabolic health and fitness, or whether sedentary time has a compounding effect over time on these outcomes requires future research. This is an important area for future research. Although this study is cross-sectional, it is the first known study to have quantified sedentary time and its relationship with health indicators in a CAD population, and does suggest a new and important area of study for this population. Further, measures of sedentary time were collected post-CR, with an average of 10 days post-graduation. This does introduce an issue with the temporality of the data collection. While this is a limitation, movement patterns are not likely to have changed dramatically within this time frame. Secondly, this study relied on movement cut-points that

were developed in healthy adult populations. Moreover, they were developed in controlled laboratory settings, whereas participants in the current study wore the accelerometers in free-living situations. It is thus possible that these cut-points may lead to some misclassification of sedentary time and MVPA. However, the use of accelerometers provides objective measurement of sedentary time and activity in a continuous pattern and is one of the greater strengths of the study. It has been shown that self-reported sedentary time may underestimate the effects of sedentary time on cardiometabolic health.[28] The sample size, although large for a clinical study, is limited in its power to detect associations between the variables (power 58-62% for correlations). Finally, the participants were classified as having controlled lipids and BP, having a high functional capacity, were highly educated and were comprised of recent CR graduates; therefore, the findings herein are not necessarily generalizable to CAD patients who have not undergone such physical activity intervention or whose risk factors are not well-controlled.

CONCLUSIONS

Cardiac rehabilitation graduates spent almost 8 waking hours/day being sedentary, accrued in approximately 14 bouts/day (~30 minutes at a time). Similar to observations from healthy populations, greater sedentary time was associated with lower functional capacity and greater BMI, independent of MVPA. Findings suggest that even among a group of post-CR individuals who are already likely more active than patients who have not undergone CR; sedentary time remains high and is associated with poorer functional capacity, suggesting a possible new area of focus for CR programs. Sedentary time may offer a unique opportunity to improve outcomes, specifically gains in cardiorespiratory fitness, one of the key indicators of CR program success. Further investigation is needed using a longitudinal or interventional study design.

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DECLARATION OF CONFLICTS OF INTERESTS

The authors declare that they there is no conflict of interest.

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Table 1. Participant characteristics

Characteristic	Total (N = 263)	Males (n = 198)	Females (n = 65)	Males vs. females
Sociodemographics				
Age (years)	63.6 ± 9.3	62.9 ± 9.3	65.7 ± 9.0	0.03
College or university, n (%)	183 (74%)	134 (72%)	49 (80%)	0.35
Married or equivalent, n(%)	183 (74%)	149 (80%)	34 (56%)	0.005
Working status				0.03
Employed full time, n (%)	82 (31%)	66 (33%)	16 (25%)	
Employed part time, n (%)	11 (4%)	7 (4%)	4 (6%)	
Self-employed	24 (9%)	23 (12%)	1 (1.5%)	
Unemployed	10 (4%)	9 (4%)	1 (1.5%)	
Retired	122 (47%)	83 (42%)	39 (60%)	
Missing	14 (5%)	10 (5%)	4 (6%)	
Clinical				
Smoker, n (%)	4 (2%)	3 (2%)	1 (2%)	0.51
Type 2 diabetes, n (%)	45 (18%)	39 (20%)	6 (9%)	0.05
Medications				
ACE-inhibitors, n (%)	153 (58%)	117 (59%)	36 (55%)	0.60
Beta-blockers, n (%)	207 (79%)	157 (79%)	50 (77%)	0.69
Statins, n (%)	242 (92%)	186 (94%)	56 (86%)	0.05
Markers of cardio-metabolic health and fitness				
Body mass index (kg/m^2)	28.2 ± 4.6	28.5 ± 4.4	27.1 ± 5.0	0.008

[n=262]				
Waist circumference (cm) [n=262]	99.5 ± 12.6	101.4 ± 12.2	93.6 ±12.2	<0.0001
Waist-to-height ratio [n=262]	0.58 ± 0.08	0.58 ± 0.08	0.58 ± 0.08	0.44
Systolic blood pressure (mm Hg) [n=261]	121 ± 18	121 ± 17	120 ± 19	0.85
Diastolic blood pressure (mm Hg) [n=262]	72 ± 10	73 ± 9	70 ± 10	0.03
HbA1c (%) [n=245]	5.9 ± 0.7	5.9 ± 0.8	5.8 ± 0.6	0.45
Total cholesterol (mmol/L) [n=259]	3.40 ± 0.82	3.28 ± 0.69	3.77 ± 0.57	0.0002
HDL (mmol/L) [n=259]	1.18 ± 0.32	1.09 ± 0.28	1.45 ± 0.29	<0.0001
LDL (mmol/L) [n=258]	1.68 ± 0.65	1.62 ± 0.56	1.87 ± 0.86	0.05
Triglycerides (mmol/L) [n=259]	1.23 ± 0.65	1.28 ± 0.72	1.11 ± 0.39	0.10
DASI score [n=216]	47.0 ± 11.5	48.5 ± 10.5	41.4 ± 13.5	0.001
Peak $\dot{V}O_2$ before CR (mL/kg/min) [n=110]	22.1 ± 5.8	23.0 ± 5.6	18.8 ± 5.6	0.003
Peak $\dot{V}O_2$ after CR (mL/kg/min) [n=168]	25.2 ± 6.6	26.2 ± 6.7	21.1 ± 4.3	<0.0001
Level of functional capacity [n=168][19, 20]				0.0005

Low (<16 mL/kg/min), n (%)	12 (7%)	7 (5%)	5 (14%)	
Moderate (16-21 mL/kg/min), n (%)	35 (21%)	21 (16%)	14 (40%)	
High (≥22 mL/kg/min), n (%)	121 (72%)	105 (79%)	16 (46%)	

Data presented as mean ± standard deviation unless otherwise specified.

CR – cardiac rehabilitation, DASI – Duke Activity Status Index, HDL – high density lipoprotein, LDL – low density lipoprotein

Table 2: Wear time and movement patterns by sex

	Mean ± standard deviation			
	Total (N=263)	**Males (n=198)**	**Females (n=65)**	**Males vs. Females**
Total wear time, minutes/day	831.6 ± 86.3	835.9 ± 84.6	818.5 ± 90.6	p=0.18
Sedentary behaviour				
Sedentary time, minutes/day	468.9 ± 92.9	483.6 ± 90.8	424.2 ± 85.2	**p<.0001**
Sedentary time, hours/day	7.8 ± 1.4	8.0 ± 1.3	7.2 ± 1.3	**p<.0001**
Sedentary bouts, number/day	13.9 ± 3.7	14.5 ± 3.6	12.0 ± 3.5	**p<.0001**
Sedentary breaks, number/day	12.8 ± 3.7	13.4 ± 3.6	11.0 ± 3.5	**p<.0001**
Activity				
Light activity, minutes/day	318.6 ± 82.6	306.3 ± 78.5	356.3 ± 84.1	**p<.0001**
Total MVPA, minutes/day	44.1 ± 26.6	46.1 ± 27.3	38.1 ± 23.7	**p=0.03**
Time in MVPA bouts, minutes/day	24.4 ± 19.7	25.8 ± 20.0	20.5 ± 18.2	p=0.05
Steps per day	7171 ± 2746	7157 ± 2715	7213 ± 2861	p=0.89

MVPA – moderate-to-vigorous intensity physical activity

Table 3: Standardized regression coefficients of total sedentary time with selected markers of cardiometabolic health and fitness

Metabolic variables	**ST adjusted for wear time**	**ST adjusted for wear time and MVPA**	**ST adjusted for age, sex, MVPA**	**ST adjusted for age, sex, medications, MVPA**	
	β, p-value	β, p-value	β, p-value	β, p-value	Adjusted R^2
Body mass index	**0.63, p=0.003**	**0.58, p=0.006**	**0.49, p=0.02**	**0.47, p=0.03**	0.09
Waist circumference	**1.85, p=0.001**	**1.74, p=0.003**	1.08, p=0.06	1.06, p=0.07	0.10
logTriglycerides	1.02, p=0.10	1.02, p=0.15	1.02, p=0.36	1.02, p=0.35	0.02
logHDL	**-1.04, p=0.005**	**-1.04, p=0.004**	-1.01, p=0.43	-1.01, p=0.36	0.28
log$\dot{V}O_{2peak}$ (n=168)	**-1.05, p=0.02**	**-1.02, p=0.048**	**-1.05, p=0.002**	**-1.05, p=0.003**	0.41

* Unstandardized regression coefficients for triglycerides, HDL and $\dot{V}O_{2peak}$ presented as 10^{eb} to enable the interpretation of these outcomes in their original units

HDL – high density lipoprotein, MVPA – moderate-to-vigorous intensity physical activity, ST – sedentary time