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Original research

Standing is not enough: A randomized crossover study on the acute cardiometabolic effects of variations in sitting in healthy young men

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ABSTRACT

Objectives: Standing desks and stability balls are increasingly popular to increase muscle activity and thereby prevent potential adverse cardiometabolic effects of prolonged sitting. The present study examined the effects of (1) sitting on a stability ball ('active sitting') and (2) hourly 10-min standing interruptions during prolonged sitting on postprandial cardiometabolic biomarkers.
Design: Experimental crossover study.
Methods: Twenty healthy-weight males (19.2 ± 0.6 years) participated randomly in three 5-h conditions: (1) sitting on an office chair (SIT), (2) sitting on a stability ball (SIT-ACTIVE) and (3) sitting with hourly 10-min standing interruptions (SIT-STAND). In each condition, participants consumed a standardized mixed meal at baseline. Hourly blood samples and pre/post saliva samples were collected and analyzed for levels of insulin, glucose and cortisol. Pre/post hemodynamic monitoring (middle finger; Nexfin-monitoring) was conducted; heart rate was measured continuously (Polar) and muscle activity (leg and lower-back, Portilab) was measured during periods of sitting (on an office chair and on a stability ball) and standing.
Results: Muscle activity and heart rate during standing periods were significantly higher than during sitting (both SIT and SIT-ACTIVE). Generalized estimating equations revealed no significant difference in any of the biomarkers between the three experimental conditions. Systolic blood pressure was lower during SIT-STAND, while stroke volume was lower during SIT-ACTIVE than during SIT. Although significant, these differences were small, approximating the day-to-day variability in blood pressure and stroke volume.
Conclusions: We conclude that hourly standing interruptions during 5 h prolonged sitting or continuously sitting on a stability ball do not significantly affect postprandial cardiometabolic biomarkers in healthy young men.
Trial registration: This trial is registered in the NTR trial register (NTRcode 5723).

Practical implications

- Periods of standing evoke significantly higher heart rate and activity of the muscles in the leg and back than periods of active sitting on a stability ball and sitting on an office chair.
- Standing interruptions and sitting on a stability ball are not adequate solutions to combat potential acute negative cardiometablic health effects of prolonged sitting.
- To improve cardiometabolic health we recommend interrupting prolonged sitting with regular moderate-to-vigorous physical activity.

1. Introduction

Recent experimental studies demonstrated that light- to moderate-intensity physical activity interruptions during 5–9 h of prolonged sitting significantly reduced postprandial glucose,[1–3] insulin[2,3] and C-peptide[4] in normal weight adults. Physical activity interruptions not only varied in intensity, but also in frequency, duration and type of physical activity, i.e. 2-min light-intensity walking interruptions every 20 min,[1,3] 1 min 40 s moderate-

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intensity walking interruptions every 30 min[2] and hourly 8-min moderate-to-vigorous cycling interruptions.[4]

Explanations for the above-mentioned effects of limiting periods of prolonged sitting on postprandial levels of glucose, insulin and C-peptide are that prolonged lack of muscle contractions in weight-bearing muscles suppresses glucose uptake, insulin sensitivity and skeletal muscle lipoprotein lipase (LPL) activity. Reduced LPL activity has been associated with impaired plasma triglyceride clearance, reduced levels of plasma high-density lipoprotein, as well as fasting blood glucose and HbA1C.[5,6] Although the frequency, intensity and duration of muscle contractions to combat such potential adverse cardiometablic effects is currently unknown, the availability and use of standing desks in offices has increased.[7]

Previous studies in overweight and obese adults demonstrated beneficial effects of standing interruptions of 5 min every 30 min on postprandial levels of glucose and insulin,[8] and of interchanging between standing and sitting every 30 min on postprandial levels of glucose.[9] However, previous studies examining the effects of standing interruptions during prolonged sitting on postprandial levels of glucose, insulin and lipids in normal weight adults demonstrated no acute effects, despite large variations in frequency and total volume of standing.[2,4,10] Miyashita et al.[10] found no differences in postprandial levels of glucose and insulin during one day of sitting with six 45-min standing interruptions compared to one day of prolonged sitting in healthy young men (aged 23–30 years). One day of sitting with 2-min standing interruptions every 20 min did not result in different postprandial area under the curve (AUC) for glucose and lipids in normal weight young adults (aged 24 ± 3 years)[2] and for glucose and insulin in normal weight men aged 30–65 years,[4] compared to one day of prolonged sitting.

Remarkably, in the study of Gao et al.,[11] 2 h of continuous standing resulted in a higher postprandial AUC for glucose (10% and 40% for total and incremental AUC, respectively) but not insulin in healthy women (aged 49 ± 8 years), when compared to 2 h of sitting. No differences were found in postprandial insulin and lipids. Gao et al.[11] additionally demonstrated a greater thigh and leg muscle activity and a higher energy expenditure, with a higher proportion of fat use and a lower proportion of carbohydrate use, during standing than sitting. Gao et al.[11] proposed that this finding suggests a fuel switch in favour of fat oxidation, yet no differences were found in postprandial lipids (i.e. triglycerides, free fatty acids, glycerol).

During sitting on a stability ball (i.e. active sitting) the leg and back muscles may elicit a low but constant level of muscle contraction, which may be sufficient to affect cardiometabolic biomarkers. Moreover, previous studies in 21–48-year-old office workers.[12] and 21–76-year-old adults[13] demonstrated significantly higher net energy expenditure (kcal/h, kcal/min) during respectively 15 and 23 min of sitting on a stability ball versus sitting on an office chair. When extrapolating their findings, Lerma et al.[13] concluded that active sitting may result in an additional energy expenditure of 247 kcal/week versus sitting on an office chair. To date no previous studies have explored the acute cardiometabolic effects of prolonged sitting on a stability ball compared to sitting on an office chair. Therefore, this study examined the effects of (1) sitting on a stability ball and (2) sitting with hourly 10-min standing interruptions, i.e. two currently popular variations in sustained sitting eliciting a minimum level of muscle contraction, on postprandial cardiometabolic biomarkers in normal weight young men. We implemented one standing interruption every hour as this is in line with our previous work,[1] and a recent study in office workers demonstrating that interrupting sitting more frequently is not representative for daily life.[14] We measured muscle activity of thigh and trunk muscles to explore potential differences in muscle activation during active sitting, standing and sitting on an office chair. We studied participants in a postprandial state as this resembles normal daily life. The importance of studying the postprandial state is emphasized by evidence that peak levels of glucose and lipids induced by high-calorie meals are associated with inflammation, endothelial dysfunction, and sympathetic hyperactivity.[15,16] Moreover, when repeated multiple times each day, these peaks in glucose and lipids increase the risk for atherosclerosis and cardiovascular diseases.[16]

2. Materials and methods

Males aged 18–22 years volunteered to participate in this study. Participants were recruited through distribution of flyers and announcements on university websites, from June 2015 to June 2016. Participants were included if they were of normal weight and apparently healthy, and were Dutch or English speaking. Exclusion criteria were major illness/injury (e.g. heart, kidney, joint, muscle or coagulation problems), diabetes mellitus type II and physical problems that may limit the ability to perform the experiment (i.e. standing interruptions or sitting on a stability ball). Participants were screened by a health-check questionnaire, including questions about medical history (e.g., heart/kidney/joint/muscle/asthmatic complaints, coagulation problems, chest pain). Females were excluded from the study as variations in levels of oestrogen and progesterone during the different phases of the menstrual cycle may influence insulin response to activity.[17,18] The study was approved by the Medical Ethics Committee of the VU University Medical Center in Amsterdam (registration number 2015.053) and was in accordance with the Declaration of Helsinki. All participants signed informed consent before participation to this study.

This crossover study included three experimental laboratory conditions of 5 h duration in a laboratory setting. The experimental conditions were: (1) prolonged sitting (SIT; i.e. on a chair with back support), (2) active sitting (SIT-ACTIVE; i.e. on a stability ball) and (3) sitting (i.e. on a chair with back support) with hourly 10-min standing interruptions (SIT-STAND). For the SIT-ACTIVE condition, when necessary the height of the stability ball was adjusted for each subject by deflating or inflating it slightly. To eliminate potential carryover effects, there was a minimum washout of 6 days between each condition. The main researcher randomly assigned the order of the experimental conditions using the random number generation function in MATLAB and revealed the order for each participant to the research assistants prior to the first experimental day of each participant. All measurements were performed by trained research assistants according to a standardized protocol. Measurements were conducted at the Amsterdam UMC, location VU University Medical Center, Amsterdam, The Netherlands, between June 2015 and July 2016.The full protocol can be obtained upon request. A completed CONSORT checklist is in Supplementary file 1.

Following completion of informed consent and health history, participants were asked to wear an accelerometer (ActiGraph GT3X+) for one week before each experimental condition, during waking hours at their right hip and during sleep hours at their non-dominant wrist, to capture their physical activity, sedentary behaviour and sleep. However, as some participants forgot to switch the accelerometer to their wrist at night, we decided to analyse accelerometer data of all participants during waking hours, i.e. between 7:00 A.M. and 23:00 P.M. Moreover, participants were requested to refrain from any moderate- to vigorous-intensity physical activity (MVPA) for at least 72 h prior to each experimental condition, and to avoid drinking alcohol and smoking for at least 24 h prior to each experimental condition. On the evening before each experimental condition participants were requested to consume a standardized meal (3 meal choices) and optional snack (1

snack choice). Participants were requested to consume the same standardized food prior to all three experimental conditions.

On the experimental days, participants arrived in the laboratory after a 10-h fast. At the start of the first experimental day, anthropometric measures were obtained with participants in light clothing. Baseline measures of autonomic functioning were obtained directly after collection of anthropometrics (for the first experimental day) or at the start of each experimental day (for the second and third experimental days). Subsequently, an in-dwelling venous catheter was inserted in the antecubital vein of the left arm to prepare for hourly blood collection, a heart rate monitor (Polar RS800CT) was fixed to the participants chest using an elastic belt to allow continuous heart rate monitoring, and surface electrodes were placed at the thigh (rectus femoris, vastus lateralis) and trunk (erector spinae) muscles to allow hourly measurement of muscle activity (Portilab, TMS 1, sample frequency 1000 Hz). After shaving and cleaning the skin with 70% ethanol, two electrodes (lead-off area 1.0 cm^2; Blue Sensor; Ambu, Ølstykke, Denmark) were placed on the belly of each muscle in a bipolar configuration (interelectrode distance of 25 mm). A reference electrode was placed on the patella. EMG recordings of 5 min were made hourly after the steady state period (i.e. 4 times) during periods of sitting (i.e. during SIT and SIT-STAND), active sitting (i.e. during SIT-ACITVE) and standing bouts (i.e. during SIT-STAND). Participants then sat quietly in a reclining chair for 1 h to achieve a 'steady state'. Next, baseline saliva and blood samples were obtained. Saliva samples were collected using a salivette cotton swab, which participants were requested to chew for approximal 60 s to stimulate salivation and subsequently return the swab with saliva to the salivette. After collection of baseline saliva and blood samples, participants consumed a standardized liquid high-fat mixed meal for breakfast within 10 min, consisting of approximately 58.8 g fat, 92.0 g carbohydrates, and 15.6 g proteins (in total 843 kcal). The content of the standardized meal was based on a previous study of our group in young adults.[1] Following consumption of the standardized meal, participants completed one of the experimental conditions for the subsequent 4 h. Participants were allowed to use the computer or tablet (e.g. watching movies, surfing on the Internet, gaming or reading) and to drink water ad libitum. During the sitting, participants were instructed to minimize movement but were allowed to visit the toilet. In the SIT-STAND condition, blood samples were obtained just before the onset of the standing period. Prior to the last blood sampling, a second saliva sample was collected. At the end of each experimental day, a second measure of autonomic functioning was obtained. Finally, participants performed a 90-s stepping task on a metronomic rhythm (120 beats per second; using a metronomic application) to enable normalization of the muscle activity data.

Anthropometric measures included weight, height, waist and hip circumference, and body fat percentage. Body weight was measured using a calibrated electronic scale (Kern MPE) with an accuracy of 0.1 kg. Height was measured twice using a Harpenden stadiometer (Holtain Ltd.) with an accuracy of 0.1 cm. The mean value of the two measures was calculated. Subsequently, BMI (kg/m^2) was calculated. Waist and hip circumference was measured using a flexible tape (Seca 201) with an accuracy of 0.5 cm. Waist circumference was measured midway between the costal border and iliac crest. Hip circumference was measured around the widest portion of the buttocks. Body fat percentage was measured with participants in a lying position using Bio-electrical Impedance Analysis (Maltron Body Composition Analyzer BF-906) with an accuracy of 0.1%.

Functioning of the autonomic nerve system was measured with participants in a lying position, using a non-invasive Nexfin hemodynamic monitor (BMEYE). Participants were connected to a Nexfin monitor by an inflatable finger cuff that was placed on the midphalanx of the middle or index finger of the left hand. The Nexfin provides a real-time continuous arterial blood pressure and beat-to-beat hemodynamic monitoring of cardiac output, using the volume clamp method and the Physiocal calibration.[19,20] Systolic and diastolic blood pressure, heart rate and stroke volume were calculated by taking the average of a time period of 5 min.

Saliva samples were centrifuged (10 min at a frequency of 1860 rpm) and subsequently stored at −80 °C. Cortisol was determined from the saliva samples, with all samples analysed in the same assay (Supported Liquid Extraction (SLE+) and LC tandem MS detection).

Plasma glucose levels were immediately assessed, within 10 s after collection, using the YSI2300 STAT Plus Analyzer (YSI, Yellow Springs) with an accuracy of 0.2 mmol/l. Blood for C-peptide, triglyceride and high-sensitive C-reactive protein (hsCRP) was sampled in heparin gel every hour, centrifuged (10 min at a frequency of 3000 rpm) and subsequently stored at −80 °C. C-peptide was analysed using an ADVIA 1650 analyser and accompanying reagents (Siemens Healthcare Diagnostics). Triglyceride was analysed using the enzymatic colorimetric GPO-PAP method (Cobas 8000). HsCRP was analysed using a turbidimetric assay (Cobas 6000). All samples were analysed in the same assay.

Raw accelerometer data were analysed using a customized software program developed in R based on the data reduction recommendations by Chinapaw et al.[21] First data was transferred in 60-s epoch. Periods of ≥60 min of consecutive zeros were considered as non-wear time and were excluded from data analysis. A minimum of eight hours of wear time per day was required to include data in the analysis.[21] A cut point of <100 counts per minute (cpm) was selected for sedentary behaviour and >1952 for MVPA.[22] A period of at least 10 consecutive minutes below 100 cpm was defined as a sedentary bout, and sedentary time accumulated in bouts of ≥10 min was defined as prolonged sedentary time.[23,24] To date, there is no consensus on the minimum duration of an MVPA bout. We defined an MVPA bout as a period of ≥5 min above 1952 cpm, as longer bouts were rare among the participants. We allowed 10% below the lower threshold with an absolute tolerance of 3 consecutive minutes to prevent too much time below the specified cut-point. Overall sedentary time and MVPA time were expressed as percentage of wear time, sedentary time and MVPA time accumulated in bouts were expressed as percentage of overall sedentary time and MVPA time, respectively.

Average heart rate during periods of sitting, active sitting and standing interruptions were calculated, excluding the time frame in which blood samples and blood pressure were obtained.

Previous studies have shown that EMG amplitude is a reliable measure of muscle activation,[25] both during short- and long-term intervals.[26] All EMG recordings were band-pass filtered (10–400 Hz) and rectified. EMG recordings were expressed as percentage of the 75th percentile of the muscle activity during the 90-s submaximal stepping activity. EMG analyses were performed in MATLAB.

Descriptive participant characteristics (mean ± SD or median [interquartile range]) were calculated for baseline measures and heart rate during periods of sitting, active sitting and standing interruptions. Paired samples t-tests, and Wilcoxon signed-rank tests for non-normally distributed data, were used to test for differences between blood values at the beginning and the end of the steady state period at each experimental condition. ANOVA general linear models, and Friedman's ANOVA for non-normally distributed data, were used to test for: (1) baseline differences in cardiometabolic biomarker (assessed from blood, saliva, autonomic functioning) between the three experimental days; (2) differences in accelerometer-based physical activity and sedentary behaviour between the weeks prior to each experimental day; and (3) differences in muscle activity and heart rate during periods of sitting on an office chair, active sitting and standing interruptions. Based on

Table 1
Baseline participant characteristics (mean ± SD or median [interquartile range]; n = 20).

Anthropometrics	Baseline
Age (years)	19.2 ± 0.6
Height (cm)	181 ± 7
Weight (kg)	72.9 ± 9.4
BMI	22.2 ± 2.5
WC/HC ratio	0.8 ± 0.1
Body fat (%)	13.5 ± 5.0

	SIT	SIT-ACTIVE	SIT-STAND
Blood and saliva[a]			
Glucose (mmol/l)	4.1 ± 0.4	4.1 ± 0.4	4.2 ± 0.3
C-peptide (nmol/l)	0.34 [0.29; 0.45]	0.38 [0.29; 0.44]	0.37 [0.31; 0.47]
Insulin (pmol/l)	39.7 [27.1; 51.3]	44.4 [34.7; 57.8]	46.6 [30.4; 59.9]
Triglyceride (mmol/l)	0.86 ± 0.26	0.84 ± 0.28	0.89 ± 0.27
hsCRP (mg/l)	0.53 [0.30; 0.74]	0.54 [0.36; 1.04]	0.48 [0.28; 0.70]
Cortisol (nmol/l)	4.6 [3.1; 8.6]	5.0 [2.6; 7.6]	4.5 [2.9; 8.5]
Autonomic functioning			
SBP (mmHg)	120 ± 16	124 ± 18	126 ± 27
DBP (mmHg)	70 ± 10	70 ± 11	72 ± 13
HR (beats/min)	65 ± 10	67 ± 11	64 ± 7.0
SV (ml)	115 ± 13	121 ± 10	115 ± 18
Accelerometer data[b]			
Total wear time (min/day)	816 ± 103	837 ± 98	825 ± 95
Nr valid days	6.2 ± 1.0	6.3 ± 0.9	5.9 ± 1.0
Total SED time (min/day)	563 ± 102	589 ± 96	569 ± 110
Prolonged SED time (min/day)	376 ± 103	389 ± 97	377 ± 103
Nr of SED bouts per day	18 ± 5	19 ± 5	18 ± 5
MVPA time (min/day)	41 ± 24	37 ± 23	42 ± 28
MVPA in 5-min bouts (min/day)	6 ± 10	5 ± 9	9 ± 15
Nr of MVPA bouts per day	0.4 ± 0.6	0.4 ± 0.7	0.5 ± 0.7
Relative to wear time			
SED time (% wear time)	69 ± 8	70 ± 9	69 ± 8
MVPA time (% wear time)	6 ± 10	5 ± 9	9 ± 15
SED time bouts of ≥10 min (% SED time)	66 ± 10	65 ± 10	65 ± 9
MVPA in bouts of ≥5 min (% MVPA time)	9 ± 15	9 ± 16	12 ± 18

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HC, hip circumference; hsCRP, high-sensitive C-reactive protein; IQR, interquartile range; MVPA, moderate-to-vigorous physical activity; SBP, systolic blood pressure; SED, sedentary; SV, stroke volume; WC, waist circumference.

[a] Due to missing, sample sizes varied between cardiometabolic markers: n = 19 for all SIT-ACTIVE samples; for hsCRP n = 18 for SIT-ACTIVE and n = 17 for SIT-STAND; for cortisol n = 17 for SIT-STAND.

[b] Accelerometer data collected during the week prior to the experimental conditions; n = 19 for data prior to SIT and SIT-STAND.

a previous experimental study in healthy young men,[1] we determined that with a sample size of 20 participants, we are able to detect differences between conditions of 10% in blood levels of glucose, C-peptide and triglycerides, at a significance level of 5% and a power of 80%.

Generalized estimating equations (GEE) were used to assess differences in each of the cardiometabolic biomarkers between the three experimental conditions (SIT, SIT-ACTIVE and SIT-STAND), using exchangeable correlation structure. This longitudinal analysis technique was used to correct for dependency within the repeated measures (i.e. five blood samples and three conditions) for each participant. As the residuals for insulin, c-peptide and hsCRP were not normally distributed, these variables were log transformed. Additionally, total area under the curve (tAUC) and incremental area under the curve (iAUC) were calculated for all hourly measured cardiometabolic biomarkers. GEE (exchangeable correlation structure) was used to assess the difference in tAUC and iAUC between the three experimental conditions. Since we used a crossover design in this study, we did not adjust for demographic variables, such as age, gender, and weight status. All statistic procedures were performed using SPSS software (version 22.0). Statistical significance was set at $p < 0.05$.

3. Results

Fig. 1 shows the flow of participants and availability of cardiometabolic biomarkers. Two participants failed to adhere to the request of arriving at the laboratory in a fasted state at the first experimental day and were excluded from the study. All participants adhered to the standardized meal prior to the experimental days, but 5 participants did not adhere to the optional snack request (4 participants consumed the snack prior to all but one day, and 1 participant consumed the snack only prior to one of the experimental days). Table 1 shows the baseline characteristics of the twenty participants who completed all three conditions. There were no statistical differences between baseline blood and saliva data, blood pressure or levels of autonomic functioning between the three conditions. Furthermore, estimates of sedentary time and MVPA time in the week prior to each experimental day, both overall as well as accumulated in bouts, were similar between the three weeks. Participants spent on average 9–10 h per day sedentary, of which 66-70% of time was accumulated in bouts of ≥10 min. MVPA time was on average 36–44 min per day, of which less than 1% was accumulated in bouts of ≥5 min.

All cardiometabolic biomarkers were similar between conditions, although insulin levels were slightly higher during SIT-STAND than during SIT (i.e. insulin levels 6.2% higher during SIT-STAND than SIT; Table 2). Additionally, for all cardiometabolic biomarkers, GEE analysis revealed no significant differences in postprandial tAUC and iAUC between the different conditions (Table 3). Systolic blood pressure was significantly lower at the end of SIT-STAND than at the end of SIT (B = −5.6, 95% CI = [−9.6; −1.6]). Stroke volume was significantly lower at the end of SIT-ACTIVE than at the end of SIT (B = −7.1, 95% CI = [−11.5; −2.7]).

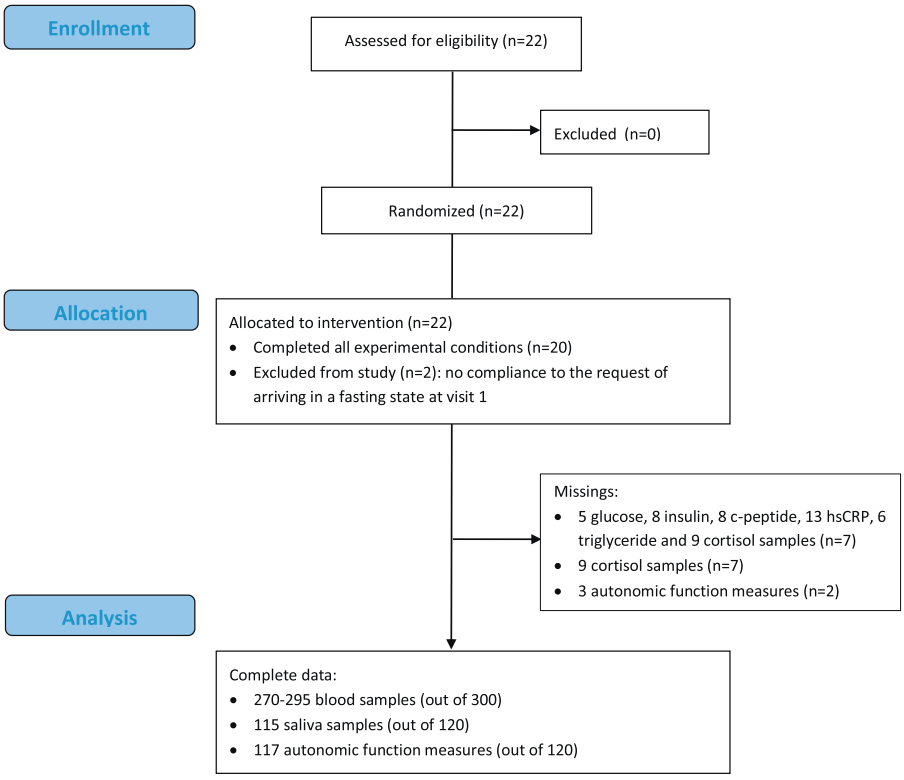

Fig. 1. Flow chart of inclusion of participants and available cardiometabolic biomarkers.

Table 2
Difference (B and 95% CI) in cardiometabolic biomarkers between SIT, SIT-STAND and SIT-ACTIVE.[a]

	SIT-ACTIVE B [95% CI]	SIT-STAND B [95% CI]
Blood[b]		
Glucose (mmol/l)	−0.07 [−0.31; 0.18]	0.06 [−0.15; 0.27]
Log c-peptide (nmol/l)	−0.02 [−0.05; 0.01]	0.04 [−0.01; 0.08]
Log insulin (pmol/l)	−0.01 [−0.06; 0.04]	0.06 [−0.00; 0.12]
Triglyceride (mmol/l)	0.04 [−0.15; 0.24]	0.08 [−0.08; 0.24]
Log hsCRP (mg/l)	0.06 [−0.06; 0.18]	−0.01 [−0.14; 0.12]
Saliva[b]		
Log cortisol (nmol/l)	−0.02 [−0.12; 0.08]	−0.003 [−0.10; 0.10]
Autonomic functioning[b]		
SBP (mmHg)	−3.6 [−9.3; 2.2]	**−5.6 [−9.6; −1.6]**
DBP (mmHg)	0.03 [−3.7; 3.8]	−2.5 [−5.2; 0.2]
HR (beats/min)	−1.1 [−5.7; 3.5]	0.3 [−4.0; 4.6]
SV (ml)	**−7.1 [−11.5; −2.7]**	−2.1 [−7.4; 3.0]

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; hsCRP, high-sensitive C-reactive protein; SBP, systolic blood pressure; SV, stroke volume.
The bold values are the significant results.
[a] Based on GEE analysis using the SIT-ONLY condition as reference; due to missings and outliers the total number of samples in the analyses varied.
[b] Note that blood samples were obtained hourly, whereas saliva samples and measures of autonomic functioning were only obtained at the beginning and the end of each condition.

Table 3
Total and incremental area under the curve for cardiometabolic biomarkers during SIT, SIT-STAND and SIT-ACTIVE.

	SIT	SIT-STAND	SIT-ACTIVE
Total AUC			
Glucose (mmol/l)	16.5 ± 1.7	16.8 ± 2.2	16.3 ± 2.4
C-peptide (nmol/l)	4.2 [3.7; 4.9]	4.5 [3.7; 5.4]	3.9 [3.5; 4.3]
Insulin (pmol/l)	759 ± 174	881 ± 304	682 ± 426
Triglyceride (mmol/l)	4.6 ± 1.3	4.9 ± 1.8	4.7 ± 1.8
hsCRP (mg/l)	2.2 [1.2; 2.9]	1.9 [1.1; 2.8]	2.2 [1.4; 4.0]
Incremental AUC			
Glucose (mmol/l)	0.5 [0.0; 1.6]	0.7 [0.3; 1.8]	0.4 [0.0; 1.3]
C-peptide (nmol/l)	2.7 [2.2; 3.3]	3.1 [2.5; 3.8]	2.5 [2.0; 2.9]
Insulin (pmol/l)	577 [470; 722]	641 [489; 908]	494 [375; 572]
Triglyceride (mmol/l)	0.6 [0.0; 1.5]	1.0 [0.0; 1.4]	1.1 [0.7; 1.9]
hsCRP (mg/l)	0.01 [0.00; 0.05]	0.01 [0.00; 0.02]	0.00 [0.00; 0.03]

Note: Values represent mean ± SD or median [interquartile range].
Abbreviations: AUC, area under the curve; hsCRP, high, sensitive C-reactive protein; iAUC, incremental AUC; IQR, interquartile range; SD, standard deviation; tAUC, total AUC.

Supplementary file 2 shows heart rate (n = 16 participants with complete data) and muscle activity (n = 7 participants with complete and reliable EMG data) during periods of sitting, active sitting and standing. Heart rate (bpm; mean ± SD) was slightly but significantly higher during standing periods (79.7 ± 10.4) than during sitting (72.0 ± 6.9 and 74.0 ± 8.6 during sitting periods in SIT and SIT-STAND, respectively; p = 0.0001). Heart rate during active sitting (73.3 ± 7.4) was not significantly different from sitting or standing. Muscle activity during standing periods was 1.7 (rectus femoris), 4.0 (vastus lateralis) and 1.8 (erector spinae) times higher than during sitting periods (p = 0.003). Muscle activity during active sitting and sitting was similar.

4. Discussion

This crossover study including twenty young healthy men demonstrated that active sitting and 10-min standing interruptions in sitting had no acute effects on cardiometabolic biomarkers, when compared to prolonged sitting. Systolic blood pressure was significantly lower following one day of hourly 10-min standing interruptions in sitting and stroke volume was significantly lower following one day of active sitting than following one day of prolonged sitting. The clinical relevance of these differences is unknown, but as the differences in systolic blood pressure and

stroke volume are small and similar to the day-to-day variability in baseline values of these measures, we doubt the clinical relevance.

To the best of our knowledge, this is the first study examining acute cardiometabolic effects of one day of active sitting compared to prolonged sitting on a chair. During sitting on a stability ball, participants' heart rate was similar to their heart rate during sitting on a chair, which is in line with previous findings in 21–48-year-old office workers.[12] The small increases in energy expenditure demonstrated during 15 min[12] and 23 min[13] of sitting on a stability ball compared to sitting on an office chair may be insufficient to affect cardiometabolic health in young men. In line with this, we found no differences in activity of the rectus femoris, vastus lateralis and erector spinae muscles during active sitting compared to sitting on an office chair. Additionally, Lerma et al.[13] found no differences in normalized (against maximal muscle contractions) upper (m. upper trapezius and m. erector spinae) and lower (m. medial gastrocnemius and m. rectus femoris) muscle activity during active sitting. Similarly, except for the left thoracic erector spinae, Gregory et al.[27] found no significant differences in normalized (against maximal muscle contractions) muscle activity of the right thoracic erector spinae, left and right lumbar erector spinae, left and right rectus abdominis and left and right external oblique between sitting on a stability ball and sitting on an office chair in young adults (aged 25.4 ± 5.4 and 22.3 ± 1.0 years old men and women, respectively). Kingma and van Dieen[28] showed in young females (aged 21.7 ± 1.6 years old) a higher normalized (against maximal muscle contractions) muscle activity of the lumbar erector spinae, but not of the thoracic erector spinae and the trapezius muscles, during sitting on a stability ball compared to sitting on an office chair. Thus, these findings suggest that muscle activity may not be sufficiently increased during active sitting compared to sitting on an office chair.

We found no acute effects of standing interruptions during prolonged sitting on postprandial levels of cardiometabolic blood markers. This is in line with previous studies demonstrating no acute effects of standing interruptions on postprandial levels of glucose, insulin and lipids in normal weight adults (age range: 21–65 years), with standing interruptions varying from 2-min interruptions every 20 min[2,4] to 45-min standing interruptions every hour.[10] Counterintuitively, Gao et al.[11] demonstrated higher levels of postprandial glucose, but not insulin and lipids, during 2 h of standing when compared to 2 h of sitting.

Similar to previous studies in healthy adults[11,12,29] heart rate was significantly higher during standing interruptions when compared to heart rate during sitting periods. In line with this, greater net energy expenditure was shown in healthy weight adults during periods of standing compared to sitting periods.[11,12,29] Additionally, we found a significantly higher muscle activity of the rectus femoris (1.7 times), vastus lateralis (4.0 times) and erector spinae (1.8 times; normalized against stepping at 120 beats per second) during active sitting compared to sitting on an office chair. Similarly, Gao et al.[11] found a 49% higher combined muscle activity (i.e. leg, thigh and back muscles; normalized against walking at 5 km/h on a treadmill) during 2 h of standing than during 2 sitting hours. In contrast, Lerma et al.[13] found no significant differences in normalized upper (m. upper trapezius and m. erector spinae) and lower (m. medial gastrocnemius and m. rectus femoris) muscle activity between 20 min of standing and 20 min of sitting on a chair.

Thus, despite slight increases in energy expenditure and muscle activity, one bout of continuous standing and standing interruptions in prolonged sitting seems insufficient for acute effects on cardiometabolic biomarkers in healthy men. It should be noted that the above-mentioned laboratory studies examined the acute effects of a 2–6-h period of prolonged sitting and sitting with standing interruptions. Longer-term effects are currently unknown. The previous reported beneficial effects of standing in overweight and obese adults[8,9] may indicate that standing interruptions during sitting may be sufficient to instigate cardiometabolic effects in populations with a reduced insulin sensitivity. Nevertheless, as previous laboratory studies in healthy adults demonstrated beneficial acute effects of physical activity interruptions during prolonged sitting (at a light[2–4] or moderate[1] intensity), we recommend to interrupt long periods of sitting with physical activity. Remarkably, despite the lack of evidence on beneficial health effects of standing interruptions in prolonged sitting, sit-standing desks are increasingly popular, in research (e.g. intervention studies) but also in practice (e.g. workplace and school settings).

A limitation of this study is that EMG data was only reliable for 7 out of 20 participants. A reason for the unreliable EMG data is that EMG measurement is very sensitive to noise, which may be caused by movement of EMG wires. Another limitation is that not all participants adhered to the optional snack request, resulting in a slightly different food intake across experimental days. However, as all participants adhered to the meal request and fasting blood levels of cardiometabolic indicators were not different between the three experimental days (i.e. conditions), we believe this only had a limited effect on our results (if any). Furthermore, the adjustment of the height of the stability ball for each subject, by deflating or inflating it, may have resulted in differences in the surface area in contact with the stability ball. As a consequence, a more deflated ball may have resulted in more stability and thereby less muscle activity. Finally, our sample of young and healthy men prohibits the generalizability of our findings to mid-aged/older populations. A strength of this study is the crossover design, with a well-balanced order of the different experimental conditions. Another strength is our sample of young and healthy weight men, limiting confounding effects such as aging and disease progressing.

5. Conclusion

We conclude that hourly standing interruptions and continuously sitting on a stability ball do not acutely affect cardiometabolic biomarkers in healthy young adults. Though standing desks and stability balls are currently quite popular both in workplace and school settings, for improvement of cardiometabolic health we recommend interrupting long periods of sitting with light or moderate-to-vigorous physical activity.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jsams.2018.12.016.

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