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Effects of reducing sedentary behavior on cardiorespiratory fitness in adults with metabolic syndrome: A 6-month RCT

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Abstract

Introduction: Poor cardiorespiratory fitness (CRF) is associated with adverse health outcomes. Previous observational and cross-sectional studies have suggested that reducing sedentary behavior (SB) might improve CRF. Therefore, we investigated the effects of a 6-month intervention of reducing SB on CRF in 64 sedentary inactive adults with metabolic syndrome in a non-blind randomized controlled trial.

Materials and Methods: In the intervention group (INT, $n = 33$), the aim was to reduce SB by 1 h/day for 6 months without increasing exercise training. Control group (CON, $n = 31$) was instructed to maintain their habitual SB and physical activity. Maximal oxygen uptake (VO_{2max}) was measured by maximal graded bicycle ergometer test with respiratory gas measurements. Physical activity and SB were measured during the whole intervention using accelerometers.

Results: Reduction in SB did not improve VO_{2max} statistically significantly (group × time $p > 0.05$). Maximal absolute power output (W_{max}) did not improve significantly but increased in INT compared to CON when scaled to fat free mass (FFM) (at 6 months INT 1.54 [95% CI: 1.41, 1.67] vs. CON 1.45 [1.32, 1.59] W_{max}/kg_{FFM}, $p = 0.036$). Finally, the changes in daily step count correlated positively with the changes in VO_{2max} scaled to body mass and FFM ($r = 0.31$ and 0.30, respectively, $p < 0.05$).

Discussion: Reducing SB without adding exercise training does not seem to improve VO_{2max} in adults with metabolic syndrome. However, succeeding in increasing daily step count may increase VO_{2max}.

KEYWORDS

cardiorespiratory fitness, cardiovascular disease, obesity, physical activity, sedentary behavior

1 | INTRODUCTION

Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors, defined as having three or more of the following: increased waist circumference (WC), elevated blood triglycerides, reduced high density lipoprotein cholesterol (HDL-C), elevated blood pressure, and elevated fasting blood glucose.[1] The estimated prevalence of MetS is 34% among US adults[2] with comparable prevalence rates reported in Finland.[3]

Poor cardiorespiratory fitness (CRF) is associated with an increased incidence of MetS.[4] Indeed, physical exercise training improves all the components of MetS,[5] and solid evidence shows that the risk of cardiovascular disease and mortality is reduced with higher CRF.[6] However, in high-income countries approximately 42% of the population is physically inactive (i.e., not meeting the guidelines of physical activity [PA]).[7] Additionally, Finnish adults spend most of their waking hours in sedentary behavior (SB)[8] which is defined as any waking behaviors with an energy expenditure of ≤1.5 metabolic equivalents (METs) while sitting, reclining, or lying.[9] Furthermore, longer duration of daily SB is associated with lower CRF, higher WC, and higher body fat percentage.[10]

Given the low adherence to PA guidelines, interventions targeted to reduce SB rather than those targeted to increase exercise training might be more attainable or favored for health promotion among people at risk for cardiovascular mortality and morbidity (i.e., individuals with MetS).[11] Speculatively, individuals with physical inactivity, high SB and poor baseline CRF might benefit from relatively light-effort PA. A recent meta-analysis of observational and cross-sectional studies showed an inverse association between device-measured SB and CRF indicating that people who accumulate more SB have lower CRF.[12] Similarly, based on cross-sectional regression modeling, one additional hour of device-measured daily SB has been associated with lower CRF in men and women (−0.12 and −0.24 METs, respectively).[13] Similar results were found in a recent cross-sectional study.[14] However, the cross-sectional and observational studies have inherent limitations for interpreting causality.

To the best of our knowledge, studies on the effects of SB reduction without increasing exercise training on CRF remain limited. Thus, the purpose of this study was to investigate whether reducing SB could improve CRF during 6 months in sedentary adults with MetS and overweight or obesity.

2 | METHODS

This study consists of secondary outcomes of a two-armed parallel group non-blind randomized controlled trial conducted at the Turku PET Centre, Turku, Finland between April 2017 and March 2020. The study was registered at Clinicaltrials.gov (NCT03101228, 05/04/2017). The study consisted of a 1-month screening phase and a subsequent 6-month intervention period. All participants gave their informed consent before entering the study. The study was conducted according to the Declaration of Helsinki, and it was approved by the Ethics Committee of the Hospital District of Southwest Finland (16/1801/2017).

2.1 | Participants

The participants in this study were recruited from the local community using newspaper advertisements and bulletin leaflets. Inclusion criteria for the participants were self-reported physical inactivity (<120 min of moderate-to-vigorous PA/week), high SB (≥10 h or 60% of daily accelerometer wear time during screening), age 40–65 years, body mass index (BMI) 25–40 kg/m^2, and MetS defined as three or more of the following five criteria: (1) WC ≥94 cm for men or ≥80 cm for women; (2) triglycerides ≥1.7 mmol/L; (3) HDL-C <1.0 mmol/L for men or <1.3 mmol/L for women; (4) resting systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg; or (5) fasting blood glucose >5.6 mmol/L.[1] Exclusion criteria were blood pressure ≥160/100 mmHg, fasting blood glucose ≥7.0 mmol/L or diagnosed diabetes, history of a cardiac disease, excessive alcohol consumption (>12 or >23 units/week for women and men, respectively), the use of narcotics or tobacco products, diagnosed depressive or bipolar disorder, previous exposure to ionizing radiation, inability to understand written Finnish, and any condition that would be hazardous for the participant or endanger the study procedure.

2.2 | Measurements

2.2.1 | Sedentary behavior and physical activity

As reported earlier, baseline SB and PA were measured for 4 weeks (screening phase), and thereafter during the whole 6-month intervention.[15] Triaxial accelerometers attached to the right hip were used (UKK AM30, UKK Terveyspalvelut Oy, Tampere, Finland during screening, and Movesense, Suunto, Vantaa, Finland during the intervention). The participants were advised to wear the accelerometer during waking hours and to remove it when going to sleep or when the device could be exposed to water. During screening, the accelerometer was attached to a flexible belt on the hip, and during the intervention a clip was used to attach the accelerometer to clothing (e.g., waistband). This approach was chosen instead of a thigh-worn sensor to enable the measurement during the whole study with no skin irritation due to the use of tape.

The accelerometer data was analyzed in 6-s epochs using a previously validated mean amplitude deviation (MAD) method.[16] This method is not dependent on the accelerometer used, as the raw acceleration data is used in the analysis.[17] PA was divided into light (LPA), moderate, and vigorous intensities. However, due to the very low amount of vigorous PA, moderate and vigorous intensities were grouped into moderate-to-vigorous PA (MVPA). LPA was defined as 1.5–2.9 METs (MAD 22.5–91.5 mg), and MVPA as ≥3.0 METs (MAD >91.5 mg). Furthermore, body posture was defined in <1.5 MET activities using the validated angle for posture estimation (APE) method.[18] Standing was defined as <11.6° deviation from the Earth's gravity vector during walking (reference vector) and >11.6° deviation from the reference vector was interpreted as SB. This method combines sitting, reclining, and lying as SB. Proportions of SB, standing, LPA, and MVPA were calculated and presented as a percentage of wear time. Finally, daily step count was calculated as reported previously.[18] A minimum of 4 days of measurement and wear time of 10–19 h/day was considered valid. The details of the accelerometer measurements have been reported elsewhere.[15]

2.2.2 | Cardiorespiratory fitness

CRF was evaluated by a graded maximal exercise test before and after the six-month intervention period on a recumbent cycle ergometer (eBike EL Ergometer with Case v6.7; GE Medical Systems Inc.). A recumbent cycle ergometer was used because echocardiography was also obtained during the exercise test (echocardiography is not reported here). After a 2-min unloaded warm-up, exercise testing was started at 25 W and the load was increased by 25 W every 3 min until volitional fatigue, medical reason for termination or refusal to continue (e.g., due to pain in the knees). The test was regarded as maximal when the respiratory exchange ratio (RER) was >1.0, a plateau in oxygen uptake was achieved or the heart rate reached ±10 beats/min of the age-predicted maximum. Maximal oxygen uptake (VO_{2max}) was measured via direct respiratory gas measurement (Vyntus CPX, CareFusion) during the graded exercise test. VO_{2max} was defined as the highest one-min oxygen uptake. VO_{2max} was presented as absolute milliliters of oxygen per minute (mL/min), as well as scaled to body mass (BM) ($mL/min/kg_{BM}$), and fat-free mass (FFM) ($mL/min/kg_{FFM}$) to account for differences in body size and composition.[19] Maximal power output (W_{max}) was calculated using the formula $W_{max} = W_{last} + (t/180 \times 25)$, where W_{last} is the last completed workload (W) and t is the number of seconds on the last, incompleted workload. W_{max} was also scaled to BM (W_{max}/kg_{BM}) and FFM (W_{max}/kg_{FFM}). Heart rate and electrocardiography (ECG) were continuously monitored during testing. Blood pressure was measured manually, the rate of perceived exertion (Borg scale 6–20), and any physical symptoms (e.g., pain) were assessed after 1 min on every load. The test was terminated by a physician if any ECG abnormalities, abnormally high blood pressure (>260 mmHg), or abnormal symptoms (e.g., chest pain) were observed.

2.2.3 | Body composition and anthropometry

BM, FFM, and body fat percentage were measured using validated air displacement plethysmography (Bod Pod, COSMED USA Inc.) after at least 4 h of fasting.[20] Height was measured with a wall-mounted stadiometer and BMI was calculated as BM (kg) / height $(m)^2$. WC was measured at the midline between the iliac crest and the lowest rib.

2.3 | Intervention

After the screening phase, eligible participants were randomized into the intervention or control group in a 1:1 ratio. Randomization was performed by a statistician separately for women and men using random permuted block randomization (block size 44) in SAS, version 9.4 for Windows.

The intervention has been described in more detail previously.[15] The aim of the intervention was to reduce SB by 1 h/day compared to the individually determined baseline during the screening phase. The INT participants were instructed by a physiotherapist at a 1-h counseling visit to replace SB with LPA, MVPA, and standing. They were instructed to maintain their usual physical exercise training habits. The ways of reducing SB were individually discussed with the participants, including, for example, using standing desks, taking the stairs instead of an elevator, standing or lightly walking during telephone calls, etc. During the 6-month intervention, the participants were contacted via telephone approximately once per month, and they visited the research center at the mid-point of the intervention to get support for meeting the individually set goals. The participants in the CON group were instructed to maintain their usual PA and SB habits.

Both the INT and CON groups wore accelerometers (Movesense, Suunto, using the ExSed algorithms) during the whole 6-month period. The accelerometers were connected to the mobile application ExSed (www.exsed.com, UKK Terveyspalvelut Oy, Tampere, Finland) to enable daily self-monitoring of PA and SB.[21] Individual daily PA and SB goals were set on the application: for the CON group the goals were equal to the results measured during screening phase, and for the INT group 1 h was reduced from SB and an equivalent amount of time was added to LPA, MVPA and standing, according to individual preferences, as described previously.[15] However, a maximum of 20 min was added to MVPA. Adherence to the intervention in was assessed by calculating the percentage of measurement days when ≥1 h SB reduction was achieved.

2.4 | Statistical analyses

Baseline characteristics are presented as mean (standard deviation [SD]) unless otherwise stated. Baseline group differences were assessed by *t*-tests in continuous variables and by Fisher's exact tests in categorical variables. All participants were analyzed in the groups that they were originally randomized into. Intervention effects were calculated using a linear mixed model for repeated measurements: using the CRF variables (VO_{2max} ml/min, ml/min/kg_{BM}, or ml/min/kg_{FFM}, or W_{max}, W_{max}/kg_{BM}, or W_{max}/kg_{FFM}) as the dependent variable and group, time, and the interaction term (group × time) as the independent variables. The linear mixed model analyses also included sex as a variable. A compound symmetry covariance structure was used for time. Multiple comparisons were adjusted with the Tukey–Kramer method. The normal distribution of the residuals was evaluated visually. Intervention effects were reported as model-based means (95% confidence interval [95% CI]). Changes during the study in the accelerometry, anthropometric, and CRF variables were calculated, and Pearson's correlation coefficients were used to assess the associations between the changes among all participants. Missing values were deleted pairwise in the correlation analyses. The percentage of days with ≥1 h SB reduction was reported as median (quartiles 1 and 3 [Q1, Q3]). To assess group differences in the percentage of measurement days when SB was reduced by ≥1 h, Wilcoxon rank sum test was used. Finally, we performed additional analyses for the participants with complete data using general linear model for repeated measurements to estimate effect size. Variables included in these analyses were the same as for the linear mixed models.

Statistical significance was set at $p < 0.05$ (two-tailed). The sample size ($n = 64$) was calculated for the primary outcome of the study (whole-body insulin sensitivity; NCT03101228). Baseline characteristics and correlations were analyzed using IBM SPSS Statistics 27.0 for macOS (IBM Corp.). The linear models were analyzed in SAS for Windows 9.4 (SAS Institute Inc.). Figures were created with Graph Pad Prism 9.3.1 for macOS (GraphPad Software).

3 | RESULTS

3.1 | Participant characteristics

Of the 263 volunteers, 151 were screened and a total of 64 participants were randomized into the INT ($n = 33$) or CON ($n = 31$) groups. Ethnicity of all participants was White European. Four participants (INT $n = 1$, CON $n = 3$) discontinued the intervention due to personal reasons or low back pain (Appendix S1: Figure S1, CONSORT Flow diagram). The groups were similar in baseline characteristics ($p > 0.05$), except for W_{max}/kg_{BM} which was higher in the CON group (Table 1).

3.2 | Intervention effects

The median percentage of days with ≥1 h SB reduction was 39 (Q1, Q3 24, 52) % in the INT group and 27 (18, 36) % in the CON group ($p = 0.010$). The accelerometry results of this study have been reported and discussed earlier.[15] The INT group reduced SB by 40 min/day and increased MVPA by 20 min whereas in the CON group SB and MVPA remained unchanged (group × time $p < 0.05$).[15] Furthermore, daily step count increased in both groups but significantly more in the INT group (group × time $p = 0.001$).[15] No statistically significant group differences were observed in standing time, LPA, or the number of sedentary breaks per day ($p > 0.05$).[15] When analyzed in quartiles of the 6-month intervention, the between-group differences in SB and MVPA were diminished after the second and third quartiles, respectively.[15] However, the between-group difference in the step count remained significant throughout the intervention.[15]

There were no statistically significant changes in absolute VO_{2max} values or VO_{2max} scaled to BM or FFM between the INT and CON groups (Figure 1A–C). Absolute or BM-scaled W_{max} values did not statistically significantly change between the INT and CON groups (Figure 1D,E). However, W_{max}/kg_{FFM} increased in the INT group compared to CON group (at 6 months INT 1.54 [95% CI: 1.41, 1.67] vs. CON 1.45 [1.32, 1.59] W_{max}/kg_{FFM}, group × time $p = 0.036$; Figure 1F). No statistically significant changes in maximal heart rate or maximal RER were observed in either of the groups (Figure 2A,B, respectively). The numerical estimates presented in Figures 1 and 2 are reported in Appendix S1: Table S1. When additional data analysis was performed with participants having all data

TABLE 1 Baseline characteristics of all participants and the intervention and control groups separately.

	Total ($n = 64$)	Intervention ($n = 33$)	Control ($n = 31$)	*p*-value*
Sex, *n* of females (%)	37 (57.8)	20 (60.6)	17 (54.8)	0.801
Age, years	58.3 (6.8)	59.3 (6.01)	57.2 (7.5)	0.223
Body mass, kg	93.2 (16.1)	92.4 (16.6)	94.1 (15.8)	0.676
BMI, kg/m^2	31.6 (4.3)	31.5 (4.0)	31.7 (4.6)	0.836
Waist circumference, cm	110.9 (11.3)	111.1 (11.6)	110.7 (11.1)	0.883
Body fat, %	43.1 (7.9)	43.1 (8.0)	43.1 (8.0)	0.997
Fat mass, kg	40.3 (10.6)	39.8 (10.4)	40.9 (11.1)	0.703
FFM, kg	52.9 (10.8)	52.6 (11.9)	53.2 (9.8)	0.807
Cardiorespiratory fitness				
VO_{2max}, mL/min	2087 (483)	2053 (534)	2120 (434)	0.601
VO_{2max}, mL/min/kg_{BM}	22.70 (4.66)	22.65 (5.05)	22.76 (4.33)	0.934
VO_{2max}, mL/min/kg_{FFM}	39.96 (6.08)	40.02 (5.89)	39.91 (6.36)	0.949
Maximal power output, W_{max}	130 (31)	128 (33)	132 (30)	0.642
Maximal power output, W_{max}/kg_{BM}	1.43 (0.35)	1.33 (0.27)	1.54 (0.41)	**0.025**
Maximal power output, W_{max}/kg_{FFM}	2.50 (0.49)	2.50 (0.45)	2.49 (0.52)	0.925
Maximal heart rate, beats/min	155 (16)	159 (15)	152 (16)	0.132
Maximal respiratory exchange ratio	1.12 (0.06)	1.13 (0.07)	1.11 (0.05)	0.376
Accelerometry				
Accelerometry, days	25.8 (3.5)	25.8 (3.7)	25.7 (3.4)	0.959
Wear time, h/day	14.54 (0.97)	14.47 (0.96)	14.60 (1.00)	0.588
Sedentary time, h/day	10.04 (1.01)	10.02 (0.92)	10.06 (1.11)	0.880
Standing time, h/day	1.79 (0.59)	1.81 (0.61)	1.76 (0.57)	0.754
LPA, h/day	1.74 (0.44)	1.67 (0.40)	1.81 (0.48)	0.231
MVPA, h/day	0.97 (0.32)	0.96 (0.31)	0.97 (0.34)	0.923
Sedentary proportion, %/wear time	69.1 (6.1)	69.2 (5.6)	69.8 (6.6)	0.768
Standing proportion, %/wear time	12.3 (3.9)	12.4 (3.9)	12.1 (3.9)	0.732
LPA proportion, %/wear time	12.0 (2.8)	11.6 (2.6)	12.4 (3.0)	0.256
MVPA proportion, %/wear time	6.7 (2.2)	6.7 (2.2)	6.7 (2.3)	0.986
Steps/day	5149 (1825)	5203 (1910)	5091 (1760)	0.808
Sedentary breaks/day	29 (8)	28 (8)	29 (8)	0.747

Abbreviations: BMI, body mass index; FFM, fat-free mass; VO_{2max}, maximal oxygen uptake; BM, body mass; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity. Presented as mean (SD) unless otherwise stated.

*Group difference as assessed by *t*-test, except for sex, where Fisher's exact test was used. Statistically significant group differences ($p < 0.05$) are bolded.

points, eta-squared for group × time ranged from 0.019 to 0.126 (Appendix S1: Table S2).

3.3 | Associations of changes in PA, SB, and CRF among all participants

The changes in SB, LPA, or MVPA did not correlate with the changes in CRF test results. The changes in the total daily step count correlated positively with the changes in VO_{2max} mL/min/kg_{BM} ($r = 0.31$, $p = 0.030$) and mL/min/kg_{FFM} ($r = 0.30$, $p = 0.042$). Furthermore, the change in the daily proportion of standing (out of accelerometer wear time) correlated negatively with VO_{2max} measures ($r = -0.33$ to -0.40, $p < 0.05$; see Appendix S1: Table S3 for all correlation coefficients).

4 | DISCUSSION

In this study, we demonstrated that a 6-month intervention that resulted in a 40 min reduction in daily SB and concomitant increase in MVPA of 20 min[15] with no deliberate increase in exercise training is not sufficient to increase VO_{2max} in physically inactive adults with MetS. Yet, the intervention resulted in a significant increase in

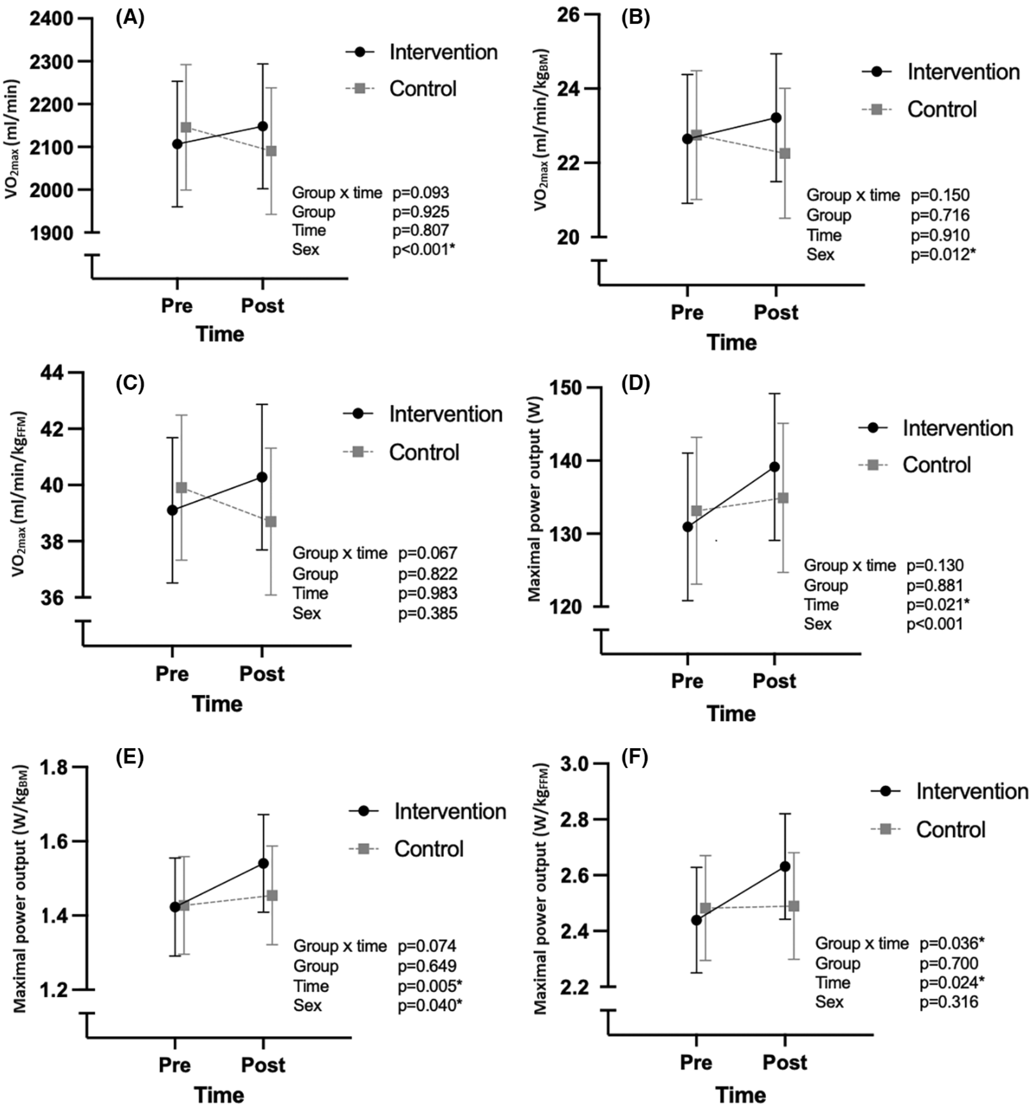

FIGURE 1 Maximal oxygen uptake (VO_{2max}) (A) without scaling, (B) scaled to body mass, (C) scaled to fat-free mass, and maximal power output (watts) (D) without scaling, (E) scaled to body mass, and (F) scaled to fat-free mass in the intervention and control groups before and after the six-month intervention. BM, body mass; FFM, fat-free mass. Values are model based means, and error bars denote 95% CIs. Solid line represents the intervention group and dashed line represents the control group. *Statistically significant ($p < 0.05$).

maximal power output scaled to FFM. However, a trend toward improved VO_{2max} and maximal power output was present in favor of the INT group, whereas a trend toward declining VO_{2max} was present in the CON group. Finally, succeeding at increasing daily step count, regardless of the original study group, may improve VO_{2max}.

The evidence from interventional studies on the effects of SB reduction on CRF is limited. However, a non-randomized pilot study by Kozey Keadle and colleagues did not observe effects on VO_{2max} from reducing SB,[22] which is in line with the present results. In The Italian Diabetes and Exercise Study 2 among individuals with type 2 diabetes, the intervention was based on both increasing MVPA and reducing SB.[23] During the 3-year intervention, VO_{2max} increased in the intervention group by 2.63 mL/min/kg_{BM} more compared to the control group.[24] After the 3-year intervention, the participants who were able to reduce SB by 0.6 or 1.5 h/day, increased their VO_{2max} by 2.61 or 4.49 mL/min/kg_{BM}, respectively.[23] Albeit the intervention also promoted increasing MVPA, most of the reduced SB was replaced by LPA.[23] However, in individuals with low CRF, the commonly used definition for LPA (i.e., 1.5–2.9 METs) might already represent moderate or vigorous intensity relative to the individual's maximal capacity.[25] In the current study, during the first 3 months, LPA increased by 19 min/day in the INT group and standing time increased slightly compared to the CON group.[26] However, during the whole intervention, the participants in the INT group of our study reduced the amount of SB by 40 min/day, on average, and it was mainly replaced by

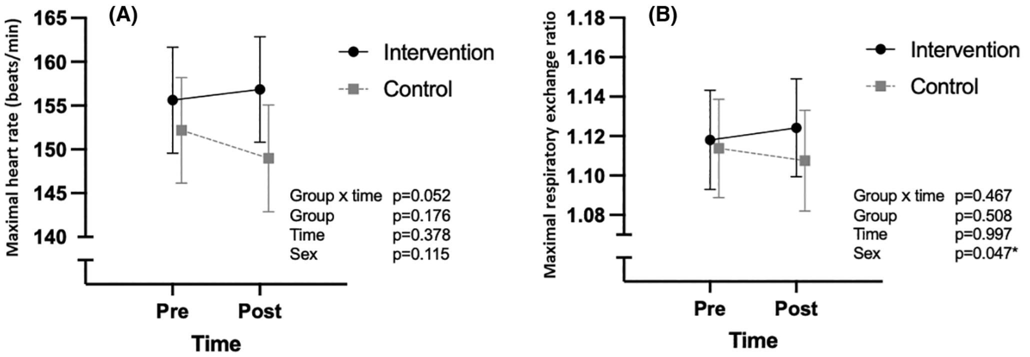

FIGURE 2 (A) Maximal heart rate and (B) maximal respiratory exchange ratio in the intervention and control groups before and after the 6-month intervention. Values are model based means, and error bars denote 95% CIs. Solid line represents the intervention group and dashed line represents the control group. *Statistically significant ($p < 0.05$).

MVPA.[15] Rest of the reduced SB was replaced by LPA and standing with no statistically significant between-group differences.[15] Interestingly, also the CON group increased the amount of MVPA during the last quartile of the intervention, which may have diluted the difference between the groups in VO_{2max} after the intervention.[15] Finally, the accelerometer data was analyzed using 6-s epochs, which capture practically all movements of the individual. Thus, the absolute minutes of PA and SB in this study should not be compared with studies that use different accelerometer methods or interpreted in the light of meeting the PA guidelines.[27]

CRF is traditionally scaled to BM. This might present issues especially in participants with overweight or obesity as adipose tissue does not considerably contribute to VO_{2max} and thus, true VO_{2max} might be underestimated.[28] Furthermore, scaling VO_{2max} to FFM instead of BM has been shown to better predict mortality.[29] Hence, scaling by FFM has been encouraged.[30] Clinically, scaling VO_{2max} by BM is highly relevant, as one has to bear the whole mass of the body in activities of daily living. However, FFM-scaling describes the potential of the cardiorespiratory system regardless of body adiposity, which, in theory, would reflect cardiovascular health. Indeed, there is evidence supporting the hypothesis that FFM-scaled VO_{2max} predicts cardiovascular outcomes better than BM-scaled VO_{2max},[29,31] whereas BM-scaling might predict outcomes that are more affected body adiposity (e.g., insulin resistance).[19] In the present study, we report absolute VO_{2max} and W_{max} values as well as results scaled to both BM and FFM. The results show that while reducing SB with no deliberate increase in exercise training is not enough to increase VO_{2max}, W_{max}/kg_{FFM} can increase indicating an improvement in the performance of the cardiovascular and musculoskeletal systems regardless of body adiposity.

It is noteworthy that the participants lost, on average, about half a kilogram of BM but there were no statistically significant between-group differences, as reported earlier.[15] FFM remained unchanged in both groups ($p > 0.05$).[15] It is widely recognized that the skeletal muscle is a significant, although not the only, tissue component of FFM. Therefore, as the skeletal muscle is the only tissue capable of force production, the observed improvements in W_{max}/kg_{FFM} in the INT group might have been because of the improved functional quality of the skeletal muscle to produce more force per kg of FFM. Furthermore, as the trend toward increased maximal heart rate after the intervention in the INT group compared to the CON group nearly reached statistical significance ($p = 0.052$, Figure 2), it is possible that the INT group participants were simply able to perform the test closer to their true maximal capacity. The reason for a group difference remains unclear, but it might be due to higher motivation in the INT group as the participants were aware of their group allocation.

Finally, along with the possibly improved functional quality of the skeletal muscles, we found that the changes in the daily step count correlated positively with the changes in VO_{2max} scaled to BM and FFM. On the other hand, the changes in the daily proportion of MVPA did not correlate with any CRF measures. This suggests that a relatively small increase in MVPA might not be sufficient to induce CRF changes, whereas increasing daily steps—consisting of both MVPA and LPA, and thus better indicating total daily PA—may lead to improvements in VO_{2max}. Interestingly, the changes in daily proportion of standing time correlated inversely with the changes in VO_{2max} (both absolute values and BM and FFM scaled values). This further emphasizes the need for more intense PA as a SB replacement in order to increase VO_{2max}. Hence, we interpret this as such that replacing SB with standing does not decrease VO_{2max} but replacing standing by MVPA might increase VO_{2max}. Nevertheless, as no analyses on individual PA and SB replacement patterns were performed, this remains only speculative.

4.1 | Strengths and limitations

Strengths of this study include a robust measurement of PA and SB with accelerometry during the whole 6-month intervention with validated[16,18] analysis methods. In addition, the randomized controlled study design enables assessing actual causality. For CRF evaluation, we used a maximal ergometry test with direct respiratory gas measurement which is considered as the gold standard method.[32] Additionally, the intervention was successful in reducing SB, as reported earlier.[15] However, only the amount of MVPA increased significantly in the INT group compared to the CON group, and the changes in LPA or standing did not differ between groups.[15] Nevertheless, the participants were not encouraged to take up any formal form of physical exercise training (e.g., jogging or participating in sports) meaning that the increased MVPA is likely a result of an increase in daily non-exercise activities. The clinical significance of the intervention effects remains elusive as, to the best of our knowledge, no evidence on the prognostic value of W_{max}/kg_{FFM} exists. Finally, the sample size was relatively small ($n = 64$) and thus, the statistical power of this study might have been inadequate to detect differences in VO_{2max} between the groups. The sample size was determined by power calculations for another outcome, whole-body insulin sensitivity, which was the primary outcome of this trial.[15]

5 | PERSPECTIVE

In physically inactive and sedentary adults with MetS and overweight or obesity, a 6-month intervention aimed at SB reduction with no deliberate increase in exercise training might not be sufficient to increase VO_{2max}. In other words, replacing SB by more intense and possibly structured PA is needed to increase CRF.

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CONFLICT OF INTEREST STATEMENT

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: J.K. received consultancy fees from GE Healthcare and AstraZeneca and speaker fees from GE Healthcare, Bayer, Lundbeck, Boehringer-Ingelheim and Merck, outside of the submitted work. The other authors report no conflicts of interest. All of the results are presented honestly with no fabrication, data falsification or inappropriate manipulation.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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