

Syddansk Universitet

Does Aerobic Exercise Increase 24-Hour Ambulatory Blood Pressure Among Workers With High Occupational Physical Activity? - A RCT

Korshøj, Mette; Krause, Niklas; Clays, Els; Søgaard, Karen; Krstrup, Peter; Holtermann, Andreas

Published in:
American Journal of Hypertension

DOI:
[10.1093/ajh/hpw197](https://doi.org/10.1093/ajh/hpw197)

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Document license
CC BY-NC-ND

Citation for published version (APA):
Korshøj, M., Krause, N., Clays, E., Søgaard, K., Krstrup, P., & Holtermann, A. (2017). Does Aerobic Exercise Increase 24-Hour Ambulatory Blood Pressure Among Workers With High Occupational Physical Activity? - A RCT. *American Journal of Hypertension*, 30(4), 444–450. <https://doi.org/10.1093/ajh/hpw197>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Does Aerobic Exercise Increase 24-Hour Ambulatory Blood Pressure Among Workers With High Occupational Physical Activity?—A RCT

Mette Korshøj,^{1,2} Niklas Krause,^{3,4} Els Clays,⁵ Karen Søgaard,⁶ Peter Krstrup,^{6,7} and Andreas Holtermann^{1,6}

OBJECTIVE

High occupational physical activity (OPA) increases cardiovascular risk and aerobic exercise has been recommended for reducing this risk. This paper investigates the effects of an aerobic exercise intervention on 24-hour ambulatory blood pressure (ABP) among cleaners with high OPA.

METHODS

Hundred and sixteen cleaners between 18 and 65 years were randomized. During the 4-month intervention period, the aerobic exercise group (AE) ($n = 57$) performed worksite aerobic exercise (2×30 minutes/week), while the reference group (REF) ($n = 59$) attended lectures. Between-group differences in 4-month ABP changes were evaluated by intention-to-treat analysis using a repeated-measure 2×2 multiadjusted mixed-models design.

RESULTS

Relative to REF, 24-hour ABP significantly increased in AE: systolic 3.6 mm Hg (95% confidence interval (CI) 1.6–5.7) and diastolic 2.3 mm Hg (95% CI 0.9–3.8). Cleaners with high aerobic workload exhibited

particularly high 24-hour ABP increases: systolic 6.0 mm Hg (95% CI 2.4–9.6), and diastolic 3.8 mm Hg (95% CI 1.3–6.4).

CONCLUSION

Aerobic exercise increased 24-hour ABP among cleaners. This adverse effect raises questions about the safety and intended benefits of aerobic exercise, especially among workers with high OPA and a demanding aerobic workload.

<http://www.controlled-trials.com/ISRCTN86682076>. Unique identifier ISRCTN86682076.

CLINICAL TRIAL REGISTRATION

Trial Number ISRCTN86682076.

Keywords: blood pressure; cleaners; hypertension; objective measurements; worksite intervention.

doi:10.1093/ajh/hpw197

Workers exposed to high occupational physical activity (OPA), such as cleaners, have an increased risk of cardiovascular disease (CVD).^{1,2} High OPA combined with low cardiorespiratory fitness,³ results in high aerobic workloads,^{4,5} that explain an increased risk for atherosclerosis,^{6,7} hypertension,⁸ and CVD.⁹

Aerobic exercise enhancing cardiorespiratory fitness has been recommended for reducing high aerobic workloads and the associated CVD risk.^{4,10} In a recent randomized controlled trial involving an aerobic exercise intervention, we observed enhanced cardiorespiratory fitness as well as reduced aerobic

Correspondence: Mette Korshøj (mkl@nrcwe.dk).

Initially submitted October 26, 2016; date of first revision December 5, 2016; accepted for publication January 6, 2017; online publication February 15, 2017.

¹National Research Centre for the Working Environment, Copenhagen, Denmark; ²Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark; ³Department of Environmental Health Sciences, Fielding School of Public Health, Southern California NIOSH Education and Research Center, University of California Los Angeles, Los Angeles, US; ⁴Department of Epidemiology, Fielding School of Public Health, Southern California NIOSH Education and Research Center, University of California Los Angeles, Los Angeles, US; ⁵Department of Public Health, Ghent University, Ghent, Belgium; ⁶Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark; ⁷Sport and Health Sciences, College of Life and Environmental Sciences, St. Luke's Campus, University of Exeter, Exeter, UK.

© The Author 2017. Published by Oxford University Press on behalf of American Journal of Hypertension, Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

workload, resting heart rate (RHR), and inflammation, but unfortunately, also increased resting systolic blood pressure (BP).^{9,11} Average 24-hour ambulatory BP (ABP) is superior to resting BP for indicating CVD risk.¹² Therefore, the aims of the present study were to investigate (i) if the aerobic exercise intervention increased ABP, and (ii) to determine if increases in ABP were particularly pronounced among workers exposed to high aerobic workloads ($\geq 30\%$ VO_2max).¹³

METHODS

The Danish Data Protection Agency and the Ethics Committee for the Capital Region of Denmark (journal number H-2-2011-116) approved the study.¹⁴ The study was a cluster-randomized controlled worksite intervention, as described elsewhere.¹⁵

Recruitment of worksites and study participants

Cleaning companies in the suburban area of Copenhagen, Denmark, were recruited. Companies were eligible to participate if they employed >50 cleaners and if cleaners were permitted to participate during paid working hours. The recruited cleaners completed a screening questionnaire, including a question about their wish to participate in the study. Eligible participants were 18–65 years old, cleaned at least 20 hours a week and provided informed consent.

Exclusions were based on pregnancy, congestive heart failure, hospital admission for myocardial infarction or acute coronary syndrome within the previous 2 years, angina pectoris, severe hypertension ($\geq 160/100$ mm Hg), serious or chronic illness, severe trauma, frequent migraine, or fever at the time of the testing. Allergy to adhesive plasters excluded diurnal measurements.

Sample size

The power calculation yielded a sample size of 52 per group to detect an expected 4% increase in cardiorespiratory fitness at an alpha level of 0.05. Assuming 40% recruitment and 30% dropout rates, we planned to enroll 130 cleaners in the study.

Randomization

Randomization was performed at cluster level, a cluster was set within strata, and strata were formed according to which manager the participant reported to. Clusters were formed by the geographical work-location, and pairwise matched on sex, age, and job seniority. The randomization was carried out by a blinded researcher and supervised by 3 researchers. All paired clusters assigned to the specific stratum were drawn from an opaque, tossed bag, and alternately allocated to either the reference (REF) or aerobic exercise group (AE), depending on the flip of a coin.¹⁵

Intervention

REF was offered 2 lectures of 2 hours duration each, not addressing physical activity. AE was offered supervised

aerobic exercise of 2 × 30 min/week in 32 sessions, at an intensity of $\geq 60\%$ maximal oxygen consumption (VO_2max), sufficient to enhance cardiorespiratory fitness.¹⁶ Through a modified intervention mapping approach¹⁷ AE was tailored to each of the enrolled companies.¹⁵ Initially, AE was offered as aerobics, cycling on a stationary bike, treadmill running, and circuit training.

Data collection

Data collection consisted of a structured interview, physical testing of health- and capacity-related measures, and objective diurnal measures of HR and ABP.¹⁵ The interview assessed demographics, job seniority, occupational and leisure time physical activity,¹⁸ smoking, diagnosed illnesses, and daily use of heart disease or antihypertension medication.

Physical tests included body weight (kg) (Tanita BC418) and height (Seca model 213 1721009). Resting BP was measured (Omron M6 Comfort) on the upper left arm after 15 minutes of sitting. Cardiorespiratory fitness was estimated using a submaximal step-test¹⁹ conducted on a bench of 30 cm height for females and 35 cm for males.¹⁵

Diurnal ABP was measured over 24 hours on a work day. ABP measurements were performed with Spacelabs 90217, (www.spacelabshealthcare.com)²⁰ mounted on the nondominant upper arm with a tube connecting cuff and sampler. Measurements were repeated every 20 minutes during waking hours and every 40 minutes during sleep.^{8,21} The participants were instructed to keep quiet and not move while the measurement was performed, to live their normal every-day life, and to keep a log of working hours, sleeping and waking times, and unmonitored periods.

HR was measured with an Actiheart monitor (www.camntech.com)²² mounted with ag-ag-cl pre-gelled electrodes (Ambu blue sensor VL-00-S/25).²³

Variable coding

Body mass index was calculated as body weight (kg) divided by squared body height (m^2).²⁴ Ethnicity was classified as western or nonwestern based on country of birth. Cardiorespiratory fitness was coded categorically in tertiles (low, medium, and high). Participants missing the cardiorespiratory fitness test constituted an additional category. ABP measurements were used for analysis if $\geq 25\%$ measurements were complete,^{20,21} corresponding to ≥ 5 during work, ≥ 8 during leisure, and ≥ 3 during sleep. Physiological outliers (systolic BP < 80 and > 240 mm Hg, diastolic BP < 50 and > 130 mm Hg) were excluded. HR was measured during the 5 minutes preceding each ABP measurement. Only HR measurements with beat error of $\leq 50\%$ were included in analysis.²⁵ HR reserve (HRR) was calculated as maximal HR (HR_{max} estimated as $208 - 0.7 * \text{age}$),²⁶ minus RHR.²⁷ RHR was defined as the 10th lowest recorded HR value during 24 hours.²³ Aerobic workload (%HRR) was calculated as $(\text{observed HR} - \text{RHR}) * 100\% / \text{HRR}$.²⁷

Statistical analysis

Analyses followed the intention-to-treat principle, including all randomized participants. Missing values were not imputed.²⁸ Within- and between-group differences in 4-month changes in ABP were computed with SEs and 95% confidence intervals (CI). Differences in 4-month ABP change were analyzed in a repeated-measures 2×2 mixed-model design. Independent categorical variables (fixed factors) were group (AE and REF), measurement time (baseline and 4-month follow-up), and interaction between group and time. Participants were entered in the model as a random effect nested in clusters. The dependent variable was 4-month ABP change and the independent variable was intervention group. The following covariates were included stepwise in the analysis (reference value in parenthesis): model 1: mean baseline ABP from the respective time period; model 2: additionally age, sex (male), daily use of antihypertension and/or heart medication (none), smoking (nonsmoker), and baseline cardiorespiratory fitness (high).

A sensitivity analysis excluded participants reporting daily use of antihypertension and/or heart medication. A subgroup analysis compared between-group changes in ABP for participants stratified by baseline aerobic workload ($\geq 30\%$ or $< 30\%$ HRR).¹³

Statistical analyses were performed using IBM SPSS statistics software (version 21) (Armonk, NY) and SAS statistical software for Windows (version 9.3) (Cary, NC).

RESULTS

Recruitment and flow

All 3 contacted companies agreed to participate. Of 250 employed cleaners, 137 (45%) consented to participate and were invited for baseline measurements. Consenters had less job seniority and were more frequently nonwestern than nonconsenters ($P < 0.05$). Baseline measurements were collected from 116

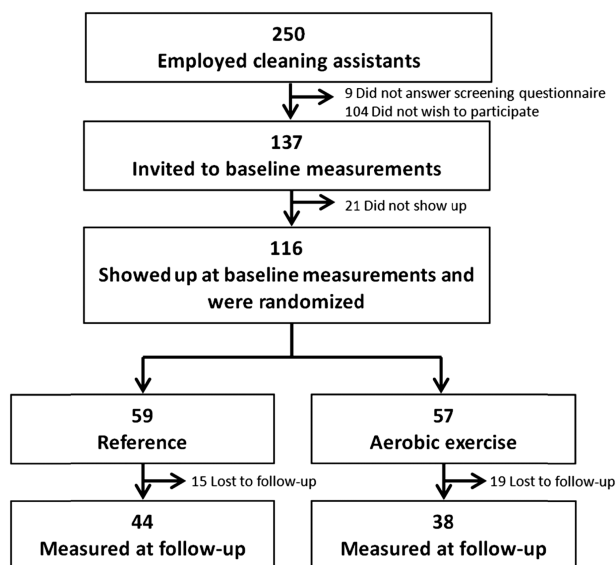


Figure 1. Flow chart of study participants.

cleaners who were randomized to REF (59) or AE (57). Thirty (26%) participants were excluded from the submaximal step-test, and 31 (27%) participants from diurnal measurements. Thirty-four (29%) participants were lost to follow-up (Fig. 1).

Adherence

Ninety-four percentage of planned sessions were offered. AE participants participated in 51% of the offered sessions, with 5 participants attended no sessions. Participants not lost to follow-up attended at least one and in total 64% of the offered sessions.

After every fourth week of intervention, HR was monitored during the aerobic exercise session; yielding an average HRR of 67% (± 13 SD).

Seventy-seven ABP measurements ($< 0.1\%$) were considered as physiological outliers and excluded from analysis.

Baseline characteristics of the study population

Table 1 presents the baseline characteristics of the study population. Education > 12 years was more prevalent in AE than REF. Participants lost to follow-up did not significantly differ by intervention group.⁹

Intervention effects

Table 2 shows crude and adjusted between-group differences in 4-month ABP changes. The fully adjusted model showed a significantly increased 24-hour ABP in AE relative to REF of 3.6 ± 1.0 mm Hg (95% CI 1.6–5.7) systolic and 2.3 ± 0.7 mm Hg (95% CI 0.9–3.8) diastolic.

When the 24 hours were divided into work, leisure, and sleep, the adjusted between-group 4-month ABP changes were: work -1.3 ± 1.3 mm Hg (95% CI -3.9 to 1.3) systolic, and -0.8 ± 0.9 mm Hg (95% CI -2.5 to 1.0) diastolic; leisure 5.5 ± 1.3 mm Hg (95% CI 2.9 to 8.2) systolic, and 3.8 ± 0.9 mm Hg (95% CI 1.9 to 5.6) diastolic; and sleep 2.9 ± 1.7 mm Hg (95% CI -0.5 to 6.4) systolic, and 2.3 ± 1.3 mm Hg (95% CI -0.1 to 4.8) diastolic (Table 2).

Sensitivity analysis

Exclusion of 14 participants reporting daily use of antihypertension and/or heart medication yielded larger between-group differences during follow-up compared to results in the entire randomized population ($N = 116$). In fully adjusted models, between-group differences in 24-hour ABP change were 5.2 ± 1.0 mm Hg (95% CI 3.2–7.2) systolic, and 3.4 ± 0.8 mm Hg (95% CI 1.9–4.9) diastolic. In this restricted subsample, relative ABP increases were also observed during working hours.

Analysis stratified by aerobic workload

The subgroup analysis stratified by baseline aerobic workload ($<$ or $\geq 30\%$ HRR during work) and adjusted for the same covariates as in Table 2 (model 2) showed that ABP among those exposed to a high aerobic workload in AE,

Table 1. Description of the randomized study population at baseline ($N = 116$), stratified by intervention group

	Randomized population ($N = 116$)			AE ($n = 57$)			REF ($n = 59$)		
	Mean	SD	n	Mean	SD	n	Mean	SD	n
Age (years)	45.3	8.6		44.9	9.2		45.7	8.1	
Sex (% of females)	75.9		88	75.4		43	76.3		45
Height (cm)	162.6	8.8		163.1	9.2		162.2	8.4	
Weight (kg)	70.7	14.1		69.7	12.7		71.7	15.4	
BMI (kg/m^2)	26.7	4.5		26.2	4.0		27.1	4.9	
Cardiorespiratory fitness ($\text{mlO}_2 \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$)	24.9	6.6		24.8	5.8		25.0	7.2	
Aerobic work load (% of HRR)	30.9	7.2		30.1	6.7		31.7	7.5	
Steps taken per working hour (steps/hour)	1316	417		1271	343		1357	473	
Job seniority (years)	11.9	7.8		12.3	8.7		11.5	6.8	
Current smoker (%)	24.1		28	22.8		13	25.4		15
Education (% with more than 12 years of education)	11.2		13	5.3*		3	16.9*		10
Ethnicity (% nonwestern)	62.1		72	70.2		40	54.2		32
Daily use of antihypertension and/or heart medication (%)	12.1		14	14.0		8	10.2		6
Leisure time physical activity (percent with <2 hour/weeks light activity or light activity 2–4 hour/weeks)	72.4		84	78.9		45	66.1		39
Physical activity at work (percent having standing/walking work including lifts and strenuous physical work)	60.3		70	63.2		36	57.6		34
Blood pressures (mm Hg)									
Resting systolic	122.3	20.1	96	122.5	23.1	45	122.2	17.3	51
Resting diastolic	80.5	12.5	96	79.9	14.2	45	81.1	10.8	51
Ambulatory systolic 24 hours	120.6	12.5	85	121.8	14.6	42	119.5	10.3	43
Ambulatory diastolic 24 hours	77.3	7.6	85	77.3	8.0	42	77.3	7.4	43
Ambulatory systolic work	122.3	13.9	65	119.6	14.4	31	124.7	13.3	34
Ambulatory diastolic work	80.2	8.2	65	78.6	9.0	31	81.6	7.3	34
Ambulatory systolic leisure	121.5	13.5	81	122.5	15.8	39	120.6	11.2	41
Ambulatory diastolic leisure	77.3	8.4	81	77.4	8.6	39	77.4	8.2	41
Ambulatory systolic sleep	107.0	11.9	67	108.0	14.6	32	106.1	9.0	34
Ambulatory diastolic sleep	65.1	7.9	67	65.4	9.2	32	64.9	6.8	34
Resting BP (≥ 140 mm Hg/ ≥ 90 mm Hg) (%)	22.9		96	20.0		45	25.5		51
ABP (≥ 135 mm Hg/ ≥ 85 mm Hg) (%)	18.8		85	23.8		42	14.0		43

Mean \pm SDs or percent (n) are reported. Differences between aerobic exercise and reference groups were analyzed with student's t -test for continuous variables, and with Chi squared test for categorical variables. Abbreviations: ABP, ambulatory blood pressure; AE, aerobic exercise; BMI, body mass index; HRR, heart rate reserve; REF, reference.

*Statistical significant difference between subgroups ($P \leq 0.05$).

compared to REF, increased by 6.0 ± 1.8 mm Hg (CI 95% 2.4–9.6) systolic, and 3.8 ± 1.3 mm Hg (CI 95% 1.3–6.4) diastolic over 24 hours; 9.6 ± 2.5 mm Hg (95% CI 4.5–14.6) systolic, and 7.8 ± 1.5 mm Hg (95% CI 4.8–10.8) diastolic during leisure; and 5.0 ± 2.4 mm Hg (95% CI 0.2–9.8) systolic, and 5.9 ± 1.9 mm Hg (95% CI 2.2–9.6) diastolic during sleep (Table 3). During work, ABP differences between subgroups were nonsignificant.

Among those exposed to low aerobic workload at baseline, the ABP between-group differences were smaller,

with only systolic ABP during leisure reaching a statistically significant increase of 4.2 ± 1.9 mm Hg (95% CI 0.4–8.0).

DISCUSSION

The main finding of this randomized controlled trial is that the aerobic exercise intervention in cleaners resulted in a significantly increased 24-hour ABP during 4 months of follow-up in AE relative to REF. The previously reported

Table 2. Within-group means pre-intervention and post-intervention, between-group (aerobic exercise group minus reference group) differences in pre-intervention to post-intervention changes of ABP

ABP (mm Hg)	AE		REF		Model 1					Model 2				
	Pre	Post	Pre	Post	Δ	SE	95% CI	P	n	Δ	SE	95% CI	P	n
24-hour														
Systolic	119.9	123.4	120.1	119.8	4.5	1.0	2.6, 6.4	<0.001	85	3.6	1.0	1.6, 5.7	<0.01	79
Diastolic	77.3	78.7	77.2	76.4	2.6	0.7	1.3, 3.9	<0.001	85	2.3	0.7	0.9, 3.8	<0.01	79
Work														
Systolic	119.8	118.3	119.4	119.6	-1.0	1.3	-3.5, 1.5	0.417	65	-1.3	1.3	-3.9, 1.3	0.33	60
Diastolic	79.4	77.8	78.9	78.5	-1.1	0.8	-2.8, 0.5	0.183	65	-0.8	0.9	-2.5, 1.0	0.40	60
Leisure														
Systolic	122.0	125.8	122.2	120.2	6.7	1.3	4.2, 9.3	<0.001	80	5.5	1.3	2.9, 8.2	<0.01	75
Diastolic	77.8	79.4	77.9	75.7	4.5	0.9	2.7, 6.2	<0.001	80	3.8	0.9	1.9, 5.6	<0.01	75
Sleep														
Systolic	108.8	108.6	107.7	105.7	3.2	1.6	0.1, 6.3	<0.050	66	2.9	1.7	-0.5, 6.4	0.10	59
Diastolic	66.4	67.0	66.1	64.6	2.3	1.1	0.1, 4.5	0.039	66	2.3	1.3	-0.1, 4.8	0.06	59

Model 1 adjusted for mean of ABP at baseline from the respective time period. Model 2 additionally adjusted for age, sex, daily use of hypertension and/or heart medication, smoking, and cardiorespiratory fitness at baseline. Abbreviations: ABP, ambulatory blood pressure; AE, aerobic exercise; CI, confidence interval; REF, reference.

Table 3. Between-group (aerobic exercise group minus reference group) differences in pre-intervention to post-intervention change of 24-hour ABP stratified by baseline aerobic workload (< or ≥30% HRR) fully adjusted for baseline values of BP, age, sex, daily use of hypertension and/or heart medication, smoking, and cardiorespiratory fitness at baseline (same as model 2 in Table 2)

ABP (mm Hg)	Aerobic workload ≥30% HRR					Aerobic workload <30% HRR				
	Δ	SE	95% CI	P	n	Δ	SE	95% CI	P	n
24-hour										
Systolic	6.0	1.8	2.4, 9.6	0.001	31	1.3	1.5	-1.7, 4.2	0.384	35
Diastolic	3.8	1.3	1.3, 6.4	0.004	31	1.1	1.1	-1.2, 3.3	0.334	35
Work										
Systolic	2.2	2.4	-2.6, 7.0	0.357	24	-4.6	2.4	-9.3, 0.1	0.054	27
Diastolic	-0.9	1.4	-3.7, 1.8	0.507	24	0.5	1.8	-3.2, 4.1	0.797	27
Leisure										
Systolic	9.6	2.5	4.5, 14.6	<0.001	30	4.2	1.9	0.4, 8.0	0.032	34
Diastolic	7.8	1.5	4.8, 10.8	<0.001	30	0.8	1.5	-2.2, 3.7	0.604	34
Sleep										
Systolic	5.0	2.4	0.2, 9.8	0.040	27	-4.7	3.3	-11.2, 1.7	0.149	25
Diastolic	5.9	1.9	2.2, 9.6	0.002	27	-2.5	2.7	-7.8, 2.8	0.356	25

Abbreviations: ABP, ambulatory blood pressure; CI, confidence interval; HRR, heart rate reserve.

increase in resting BP following this aerobic exercise intervention⁹ is confirmed by these 24-hour ABP findings.

The average adjusted between-group differences in 24-hour ABP change ranged from 2.3 mm Hg diastolic to 3.6 mm Hg systolic (Table 2), and up to 9.6 mm Hg systolic during leisure in subgroup analyses. Although the small size of the population limits the precision of estimates, the observed unintended ABP increases in AE up to 9.6 mm Hg were highly statistically significant ($P < 0.001$). This increase in ABP could translate

into a 20–40% increased CVD risk based on the known hazards of BP increases in population-based studies.^{29–31}

Between-groups differences in 4-month ABP change were relatively small during work but rather large during both leisure and sleep. These results cannot be explained by pre-post intervention changes in physical activity at work or during leisure because the number of objectively measured steps per hour during work and leisure did not change during follow-up. The relatively small ABP changes during work

may be explained by the significantly reduced aerobic workload previously reported.⁹

Analyses stratified by aerobic workload at baseline (%HRR during work) showed that those in AE exposed to high aerobic workloads experienced the highest increases in ABP over 24 hours during leisure and sleep, whereas ABP during work was unaltered (Table 3). These increases do raise concerns about the intended benefit of an aerobic exercise intervention in workers exposed to high aerobic workloads.

The results are in line with the hypothesis of Krause *et al.*⁷ that workers exposed to high OPA may overload the cardiovascular system if exposed to additional physical activity. Such an overload is plausible if there is already an imbalance between workers' cardiorespiratory fitness (capacity) and their physical work demands as well as limited possibilities for recovery. Hence, this study provides additional empirical evidence that aerobic exercise interventions among workers exposed to high OPA might overload the cardiovascular system and increase the risk of atherosclerosis, CVD, and mortality.^{6–9} The net effect on CVD risk from the previously reported enhanced cardiorespiratory fitness, reduced aerobic workload, RHR, and level of inflammation^{9,11} combined with the potentially damaging increases in ABP can only be determined in larger longitudinal studies with CVD endpoints. However, the present findings indicate a need for more focus on interventions aimed at reducing aerobic workloads. Meanwhile, we recommend that aerobic exercise interventions among those exposed to high OPA should monitor BP, preferably by 24-hour ABP, because the strongest adverse ABP increases were seen during leisure.

To our knowledge, no other physical activity intervention studies have evaluated effects on ABP.

Strengths and limitations

The strengths of this paper are: (i) the high reliability and validity of the objective diurnal field measurement, reducing the risk of bias from self-reporting, and/or differential misclassification, (ii) the cluster-randomized controlled trial design, reducing contamination bias, (iii) the mixed-model analysis without imputation,²⁸ and (iv) the comprehensive assessment and control of potential confounders during follow-up.

Exclusions based on low quality of diurnal data could have introduced selection bias. However, a differential bias is unlikely since exclusions based on quality of data were minimal (<0.01% of all ABP measurements) and equally distributed across intervention groups.

An overall 29% drop-out is to be expected in interventions during work, and are in line with presumptions,¹⁵ but needs to be considered as a possible source of selection bias. More subjects ($n = 19$) were lost to follow-up in AE than in REF ($n = 15$) and those lost to follow-up had lower cardiorespiratory fitness and higher mean aerobic workload at baseline compared to participants not lost to follow-up. This may have caused a selection bias toward a more healthy population being followed up, possibly indicating an underestimation of increase in 24-hour ABP which was especially pronounced among those with high aerobic workloads.

The sensitivity analysis excluding the 14 participants using antihypertension and/or heart medication showed larger between-group differences in 24-hour ABP (5.2 ± 1.0 mm Hg (CI 95% 3.2–7.2) systolic and 3.4 ± 0.8 mm Hg (CI 95% 1.9–4.9) diastolic) compared to the results in the entire randomized population. This could indicate that participants not using antihypertension and/or heart medication may be more prone to unintended consequences of exercise interventions than participants not undergoing medical treatment.

In conclusion, the results support the hypothesis that an aerobic exercise intervention increases 24-hour ABP among workers with high OPA. The hypothesis that the largest ABP increases occur among workers exposed to high relative aerobic workloads was also supported. The overall risks and benefits of aerobic exercise interventions need to be evaluated in prospective studies that monitor ABP not only at work but also during leisure and sleep where this study observed the greatest changes in ABP.

ACKNOWLEDGMENTS

A special thanks to Mark Lidegaard for his assistance with data collection. Also, thanks to: data manager Lisbeth Nielsen; statistician Hans Bay; and senior researcher and engineer Jørgen Skotte. The study was funded by the Danish Working Environment Research Fund (journal number 20100019624/5).

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

- Li J, Loerbroks A, Angerer P. Physical activity and risk of cardiovascular disease: what does the new epidemiological evidence show? *Curr Opin Cardiol* 2013; 28:575–583.
- Sjögren B, Fredlund P, Lundberg I, Weiner J. Ischemic heart disease in female cleaners. *Int J Occup Environ Health* 2003; 9:134–137.
- Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. The interplay between physical activity at work and during leisure time—risk of ischemic heart disease and all-cause mortality in middle-aged Caucasian men. *Scand J Work Environ Health* 2009; 35:466–474.
- Louhevaara V. Job demands and physical fitness. In Karwowski W, Marras WS (eds), *The Occupational Ergonomics Handbook*. CRC Press LLC: Boca Raton, 1999, pp. 261–273.
- Karlqvist L, Leijon O, Härenstam A. Physical demands in working life and individual physical capacity. *Eur J Appl Physiol* 2003; 89:536–547.
- Glagov S, Zarins C, Giddens DP, Ku DN. Hemodynamics and atherosclerosis. Insights and perspectives gained from studies of human arteries. *Arch Pathol Lab Med* 1988; 112:1018–1031.
- Krause N, Brand RJ, Kaplan GA, Kauhanen J, Malla S, Tuomainen TP, Salonen JT. Occupational physical activity, energy expenditure and 11-year progression of carotid atherosclerosis. *Scand J Work Environ Health* 2007; 33:405–424.
- Clays E, De Bacquer D, Van Herck K, De Backer G, Kittel F, Holtermann A. Occupational and leisure time physical activity in

- contrasting relation to ambulatory blood pressure. *BMC Public Health* 2012; 12:1002.
9. Korshøj M, Lidegaard M, Skotte JH, Krstrup P, Krause N, Søgaard K, Holtermann A. Does aerobic exercise improve or impair cardiorespiratory fitness and health among cleaners? A cluster randomized controlled trial. *Scand J Work Environ Health* 2015; 41:140–152.
 10. Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Physical demands at work, physical fitness, and 30-year ischaemic heart disease and all-cause mortality in the Copenhagen Male Study. *Scand J Work Environ Health* 2010; 36:357–365.
 11. Korshøj M, Ravn MH, Holtermann A, Hansen ÅM, Krstrup P. Aerobic exercise reduces biomarkers related to cardiovascular risk among cleaners: effects of a worksite intervention RCT. *Int Arch Occup Environ Health* 2016; 89:239–249.
 12. Hansen TW, Kikuya M, Thijs L, Björklund-Bodegård K, Kuznetsova T, Ohkubo T, Richart T, Torp-Pedersen C, Lind L, Jeppesen J, Ibsen H, Imai Y, Staessen JA. Prognostic superiority of daytime ambulatory over conventional blood pressure in four populations: a meta-analysis of 7,030 individuals. *J Hypertens* 2007; 25:1554–1564.
 13. Bonjer FH. *Encyclopedia of Occupational Health and Safety*. International Labour Organisation: Geneva, 1971.
 14. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310: 2191–2194.
 15. Korshøj M, Krstrup P, Jørgensen MB, Prescott E, Hansen ÅM, Kristiansen J, Skotte JH, Mortensen OS, Søgaard K, Holtermann A. Cardiorespiratory fitness, cardiovascular workload and risk factors among cleaners; a cluster randomized worksite intervention. *BMC Public Health* 2012; 12:645.
 16. Davies CT, Knibbs AV. The training stimulus. The effects of intensity, duration and frequency of effort on maximum aerobic power output. *Int Z Angew Physiol* 1971; 29:299–305.
 17. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. *Health Educ Behav* 1998; 25:545–563.
 18. Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation* 1968; 38:1104–1115.
 19. Aadahl M, Zacho M, Linneberg A, Thuesen BH, Jørgensen T. Comparison of the Danish step test and the watt-max test for estimation of maximal oxygen uptake: the Health 2008 study. *Eur J Prev Cardiol* 2013; 20:1088–1094.
 20. Baumgart P, Kamp J. Accuracy of the SpaceLabs Medical 90217 ambulatory blood pressure monitor. *Devices Technol* 1998; 3:303–307.
 21. Clays E, Leynen F, De Bacquer D, Kornitzer M, Kittel F, Karasek R, De Backer G. High job strain and ambulatory blood pressure in middle-aged men and women from the Belgian job stress study. *J Occup Environ Med* 2007; 49:360–367.
 22. Barreira TV, Kang M, Caputo JL, Farley RS and Renfrow MS. Validation of the actiheart monitor for the measurement of physical activity. *Int J Exerc Sci* 2009; 2:60–71.
 23. Brage S, Brage N, Franks PW, Ekelund U, Wong MY, Andersen LB, Froberg K, Wareham NJ. Branched equation modeling of simultaneous accelerometry and heart rate monitoring improves estimate of directly measured physical activity energy expenditure. *J Appl Physiol* (1985) 2004; 96:343–351.
 24. Canoy D. Distribution of body fat and risk of coronary heart disease in men and women. *Curr Opin Cardiol* 2008; 23:591–598.
 25. Skotte J, Korshøj M, Kristiansen J, Hanisch C, Holtermann A. Detection of physical activity types using triaxial accelerometers. *J Phys Act Health* 2014; 11:76–84.
 26. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol* 2001; 37:153–156.
 27. Karvonen MJ, Kentala E, Mustala O. The effects of training on heart rate; a longitudinal study. *Ann Med Exp Biol Fenn* 1957; 35:307–315.
 28. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol* 2013; 66:1022–1028.
 29. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360:1903–1913.
 30. He J, Whelton PK. Elevated systolic blood pressure and risk of cardiovascular and renal disease: overview of evidence from observational epidemiologic studies and randomized controlled trials. *Am Heart J* 1999; 138:211–219.
 31. Conen D, Bamberg F. Noninvasive 24-h ambulatory blood pressure and cardiovascular disease: a systematic review and meta-analysis. *J Hypertens* 2008; 26:1290–1299.