FYSISKE ARBEJDSKRAV OG FITNESS – BETYDNING FOR HJERTEKARSYGDOM

Slutrapport til Arbejdsmiljøforskningsfonden
(Projekt 1-2010-03)

Mette Korshøj og Andreas Holtermann

FORSKNINGSCENTER FOR ARBEJDSMILJØ

DET NATIONALE FORSKNINGSCENTER
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Titel	Fysiske Arbejdskrav og Fitness – Betydning for hjertekarsygdom
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Forord

Med denne rapport afslutter vi et forskningsprojekt, som havde det overordnede formål, at skabe ny og forbedret viden om hård fysisk aktivitet i arbejde øger risiko for hjertekarsygdom samt at undersøge forebyggende faktorer for hjertekarsygdom i relation til hård fysisk aktivitet i arbejde – deriblandt høj kondition.

Vi takker Arbejdsmiljøforskningsfonden for den bevilgede støtte til projektet og for det gode og konstruktive samarbejde under hele projektforløbet. Vi ønsker også at takke vores videnskabelige samarbejdspartnere og følgegruppe for værdifulde bidrag igennem hele projektforløbet. En særlig tak går til de virksomheder og medarbejdere, der har deltaget i projektet, samt samarbejdspartnere i Copenhagen Male Study, Østerbroundersøgelsen og Den Nationale Arbejdsmiljøkohorte.

Vi håber, at den nye viden, som projektet har skabt, vil give arbejdsmiljø- og sundhedsprofessionelle, socialrådgivere og arbejdsmarkedets parter et forbedret grundlag til at arbejde med forebyggelse af hjertekarsygdom blandt medarbejdere med hård fysisk aktivitet i arbejdet.

Forskningen i forståelsen og forebyggelsen af hjertekarsygdom i relation til hård fysisk aktivitet i arbejde fortsættes på Det Nationale Forskningscenter for Arbejdsmiljø (NFA). Vi er i gang med nye projekter, som både omhandler hård fysisk aktivitet i arbejde og stillesiddende arbejde. Projekterne bygger på erfaringer og indsigter erhvervet gennem dette projekt.

Mette Korshøj og Andreas Holtermann
Det Nationale Forskningscenter for Arbejdsmiljø
København, juli 2015

SAMMENFATNING

Formål

Projektets overordnede formål var at skabe ny og forbedret viden om, hård fysisk aktivitet i arbejde øger risikoen for hjertekarsygdom samt at undersøge forebyggende faktorer for hjertekarsygdom i relation til hård fysisk aktivitet i arbejde – deriblandt høj kondition og fysisk aktivitet i fritiden.

Metoder

Projektet var opdelt i to delprojekter:

Prospektive epidemiologiske undersøgelser (Delprojekt 1)

Formålet i projektet var at undersøge sammenhængen mellem hård fysisk aktivitet i arbejde og hjertekarsygdom og betydningen af fysisk aktivitet i fritiden og kondition herfor i tre eksisterende større datasæt (Copenhagen Male Study, Østerbroundersøgelsen, Den Nationale Arbejdsmiljøkohorte) med registerbaseret opfølgning på død fra iskæmisk hjertesygdom og generel hjertesygdom, hjerteinfarkt og død af alle årsager.

Interventionsundersøgelsen (delprojekt 2)

Formålet med interventionsundersøgelsen var at undersøge, hvorvidt en arbejdspladsintervention med konditionstræning blandt kvinder med hård fysisk aktivitet i arbejde reducerede risikofaktorer for hjertekarsygdom. De evaluerede risikofaktorer var kondition, hvilepuls, pulsbelastning under arbejde, blodtryk og inflammationsniveau. Arbejdspladsinterventionen blev udviklet i tæt samarbejde med de deltagende virksomheder og blev evalueret ved objektive døgnmålinger og blodprøver.

Resultater

Delprojekt 1

- Hård fysisk aktivitet i arbejdet synes at forøge risikoen for død fra iskæmisk hjertesygdom og generel hjertesygdom, hjerteinfarkt og død af alle årsager blandt mænd. Den samme forøgede risiko i forbindelse med hård fysisk aktivitet i arbejdet blev ikke fundet blandt kvinder.
- Uanset fysiske krav i arbejdet reduceres risikoen for at dø af iskæmisk hjertekarsygdom betydeligt, hvis man er fysisk aktiv i fritiden.
- Høj kondition synes at beskytte mod tidlig død af iskæmisk hjertekarsygdom i forbindelse med hård fysisk aktivitet i arbejde.

Delprojekt 2

Arbejdspladsinterventionen efter 4 måneder

- øgede konditionen med 9 %
- sænkede pulsbelastningen under arbejde med 11 %
- øgede det systoliske hvileblodtryk med 3 % (3,6 mmHg) og ændrede ikke det diastoliske hvileblodtryk
- sænkede hvilepuls og puls under søvn med henholdsvis 5 og 8 %
- sænkede inflammationsniveauet, målt via fald i koncentrationen af høj sensitiv C-reaktiv protein på 37 %
- øgede døgnblodtrykket, både systolisk 3 % (3,6 mmHg) og diastolisk 3 % (2,3 mmHg).

Arbejdspladsinterventionen efter 12 måneder

- øgede konditionen med 9 %
- sænkede pulsbelastningen under arbejde med 7 %
- ingen signifikante ændringer i hvileblodtryk
- sænkede hvilepulsen med 7 %, men ingen ændring i puls under søvn
- sænkede inflammationsniveauet, målt via fald i koncentrationen af høj sensitiv C-reaktiv protein med 44 %
- ingen signifikante ændringer i døgnblodtrykket.

Perspektivering

Overordnet viser projektet, at hård fysisk aktivitet i arbejdet synes at forøge risikoen for hjertekarsygdom og tidlig død blandt mænd, men ikke blandt kvinder. Både høj fysisk aktivitet i fritiden og højt kondition synes at være beskyttende faktorer for hjertekar-sygdom og dødelighed fra hård fysisk aktivitet i arbejdet.

Arbejdspladsintervention med konditionstræning blandt rengøringsassistenter viste, at den giver en række positive effekter på risikofaktorer for hjertekarsygdom såsom øget kondition, sænket pulsbelastning under arbejde, reduceret puls under hvile og søvn og sænket inflammationsniveau, dog med en stigning i blodtrykket under hvile og henover døgnet.

Samlet set, understøtter projektet vigtigheden af hård fysisk aktivitet i arbejdet for hjertekarsygdom og dødelighed, og den beskyttende helbredseffekt af høj kondition og fysisk aktivitet i fritiden for personer med hård fysisk aktivitet i arbejdet.

Konditionstræningen i arbejdstiden gav en række positive effekter, men også en negativ helbredseffekt. Vort forslag om at opnå udelukkende positive helbredseffekter fra denne type sundhedsfremme blandt medarbejdere med hård fysisk aktivitet i arbejdet vil være at integrere konditionstræning med ergonomiske og/eller organisatoriske tiltag, der er med til at reducere arbejdsbelastningen og sikre tilstrækkelig restitution og hvile. Dette er dog ikke undersøgt i dette projekt, men behøves afprøvet i fremtidige studier.

Vi håber, at den nye viden, som projektet har skabt, vil give arbejdsmiljø- og sundhedsprofessionelle, socialrådgivere og arbejdsmarkedets parter et forbedret grundlag til at arbejde med forebyggelse af hjertekarsygdom blandt medarbejdere med hård fysisk aktivitet under arbejdet.

Forskningen i forståelsen og forebyggelsen af hjertekarsygdom i relation til hård fysisk aktivitet i arbejdet fortsættes på Det Nationale Forskningscenter for Arbejdsmiljø (NFA). Vi er i gang med nye projekter, der både omhandler hård fysisk aktivitet i arbejdet og stillesiddende arbejde. Projekterne bygger på erfaringer og indsigter erhvervet gennem dette projekt.

ENGLISH SUMMARY

Purpose

The overall aim of the project was to generate novel and improved knowledge about occupational physical activity (OPA) and risk for cardiovascular disease (CVD), and to investigate preventive measures for CVD among workers with high OPA, like high cardiorespiratory fitness and physical exercise.

Methods

The project consisted of two sub-projects:

Prospective observational studies (sub-project 1)

The aim was to investigate the prospective association between OPA and CVD, and the potential moderating effect of leisure time physical activity (LTPA) and cardiorespiratory fitness on this association in three larger Danish prospective cohorts (Copenhagen Male Study, Copenhagen City Heart Study and the Danish Work Environment Cohort Study) with register-based follow-up ischemic heart disease (IHD) mortality, CVD mortality and all-cause mortality.

Intervention study (sub-project 2)

The aim was to investigate whether an aerobic exercise worksite intervention among cleaners would improve or impair risk factors for CVD. The sub-project was a 12-month cluster-randomized aerobic exercise worksite intervention. The intervention was developed in close collaboration with the participants, and accounted for the context of the specific worksites. The effects were evaluated with objective physiological or diurnal data in an intention-to-treat analysis using multi-adjusted mixed models.

Results

Sub-project 1

- High OPA seems to be positively associated with the risk of IHD mortality, CVD mortality and all-cause mortality among males. This positive association was not found among females.
- High LTPA lowered the risk of IHD mortality for all levels of OPA
- High cardiorespiratory fitness reduces the risk of IHD mortality among males with high OPA

Sub-project 2

- The intervention led to several improvements in risk factors for CVD, e.g. enhanced cardiorespiratory fitness, reduced resting and sleeping heart rate, relative aerobic workload and level of high sensitive C-reactive protein.
- The intervention elevated resting and 24-hour ambulatory blood pressure at 4-months follow-up.
- Stratified analysis on high vs low (≥/< 30 % VO_2max) relative aerobic workloads, showed that cleaners exposed to high relative aerobic workloads obtained more pronounced increases of resting and 24-hour ambulatory blood pressure, an

unaltered cardiorespiratory fitness and a reduced sleeping heart rate at 4-months follow-up.

Perspectives

Overall, the project shows that high OPA seems to increase the risk for IHD, CVD and all-cause mortality among males, but not females. Both high LTPA and cardiorespiratory fitness were observed to be protective for IHD, CVD and all-cause mortality from high OPA. The workplace intervention showed several improvements in risk factors for CVD.

Overall, the project highlights the importance of OPA for CVD and mortality, and the protective effects of high LTPA and cardiorespiratory fitness.

The aerobic exercise generated positive effects, but also enhanced the blood pressure at 4-months follow-up. Thus, the results from the worksite intervention points to the relevance of targeting reductions in the relative aerobic workload, because of the improvement in cardiovascular health, especially among those participants exposed to low relative aerobic workloads. Multifaceted interventions might be more successful in reducing the risk of cardiovascular disease among workers with high occupational physical activity.

It's our hope, that the novel knowledge from the project can provide a better foundation for work-environment and health professionals to prevent CVD and premature mortality among workers with high OPA.

INDHOLD

INDLEDNING

Baggrund

Der er stærk evidens for at fysisk aktivitet i fritiden virker forebyggende for udvikling af hjertekarsygdomme og sænker dødeligheden (1-5). Derimod er der indikationer for, at hård fysisk aktivitet i arbejdet ikke har den samme effekt på hjertekarsygdomme, og nogle studier viser, at det øger risiko for hjertekarsygdomme (6-11). Ved projektets start i 2010 var sammenhængen mellem hård fysisk aktivitet i arbejdet og hjertekarsygdomme i meget begrænset omfang undersøgt og uafklaret (8, 12, 13). Fordi en betydelig andel af erhvervsaktive i Danmark stadig har hård fysisk aktivitet i arbejdet, og personer med hård fysisk aktivitet i arbejdet generelt har en overhyppighed af hjertekarsygdomme, vurderede vi, at det var vigtigt at undersøge, om hård fysisk aktivitet i arbejdet øger risikoen for hjertekarsygdomme blandt erhvervsaktive i Danmark.

Den potentielle øgede risiko for hjertekarsygdomme fra hård fysisk aktivitet i arbejdet er foreslået at være forklaret gennem en langvarig overbelastning (stress) på hjertekar-systemet, som derved kan forårsage åreforkalkning og hjertekarsygdom (10, 13, 14). I modsætning til hård fysisk aktivitet i arbejdet reducerer fysisk aktivitet i fritiden risikoen for hjertekarsygdom (1-5). Under fysisk aktivitet i fritiden øges både puls og blodtryk akut, da disse akutte effekter stresser hjertekarsystemet (15). I pauserne mellem den fysiske aktivitet i fritiden genopbygges kroppen og kapaciteten øges for dermed at kunne kapere den fysiske aktivitet bedre. Gentagen fysisk aktivitet i fritiden medfører derfor adaptationer i hjertekarsystemet, som øger konditionen samt sænker hvilepuls og blodtryk (15-17). Disse adaptationer medfører derved et sundere hjertekarsystem og mindsker derfor risikoen for hjertekarsygdom (18-20).

Kondition, målt som den maksimale iltoptagelse per kg kropsvægt per minut, er en veldokumenteret stærk prædiktor for risikoen for hjertekarsygdom og død af alle årsager (21, 22). Yderligere har konditionen over flere årtier været anset for at være en afgørende faktor for at være i stand til at udføre hård fysisk aktivitet i arbejdet (23) men også for at klare belastningen helbredsmæssigt. Det er nemlig velkendt, at belastningen af hjertekarsystemet ved en givet fysisk arbejdsopgave er afhængig af konditionen (24, 25). Belastningen på hjertekarsystemet under fysisk aktivitet afhænger dermed af, hvilken kapacitet personens hjertekarsystem har. Den maksimale kapacitet af en persons hjertekarsystem kan beskrives som konditionen. En person med en høj kondition vil derfor ikke bruge så stor en del af sin kapacitet på at udføre en given fysisk arbejdsopgave, som en person med en lavere kondition.

Det er anbefalet af ILO, at belastningen af kroppen i gennemsnit ikke bør overstige 1/3 af ens kondition - henover en arbejdsdag på 8 timer (26). Det er derfor teoretisk arbejds-fysiologisk velbegrundet, at konditionen er vigtig i relation til de helbredsmæssige konsekvenser fra hård fysisk aktivitet i arbejde. Der mangler dog studier, der undersøger om høj kondition kan være en beskyttende faktor for hjertekarsygdom ved hård fysisk aktivitet i arbejde (27).

Det har været antaget og foreslået, at personer med hård fysisk aktivitet under arbejde bør holde sig i ro og slappe af i fritiden pga. en eventuel sundhedsskadelig effekt (13). På den anden side ville man antage, at de positive effekter af fysisk aktivitet i fritiden kan opnås af alle, uanset niveau af fysisk aktivitet i arbejde. Eksempelvis kunne fysisk aktivitet i fritiden blandt personer med hård fysisk aktivitet i arbejdet eventuelt øge deres kondition og dermed sænke pulsbelastningen under arbejdet og herved risikoen for hjertekarsygdom. Der er dog behov for at undersøge, både i observationelle kohortestudier og i interventionsstudier, om personer med hård fysisk aktivitet i arbejdet bør anbefales at være yderligere fysisk aktive i deres fritid.

Projektets formål

Det overordnede formål i projektet var at skabe ny og bedre viden om, hård fysisk aktivitet i arbejdet øger risikoen for hjertekarsygdomme, samt at undersøge om høj fysisk aktivitet i fritiden og høj kondition beskytter mod hjertekarsygdomme forårsaget af hård fysisk aktivitet i arbejdet.

Dette overordnede formål blev undersøgt i to delprojekter med følgende specifikke formål og hypoteser:

I **delprojekt 1** var formålet – gennem analyser af eksisterende prospektive datasæt – at undersøge to hypoteser:
Hypotese A: Hård fysisk aktivitet i arbejdet øger risiko for hjertekarsygdom.
Hypotese B**:** Høj fysisk aktivitet i fritiden og høj kondition modificerer sammenhængen mellem hård fysisk aktivitet i arbejdet og hjertekarsygdom.
I **delprojekt 2** var formålet – gennem en arbejdspladsintervention med konditionstræning blandt rengøringsassistenter – at undersøge følgende hypoteser:
Hypotese A: Interventionen vil øge konditionen og sænke pulsbelastningen under arbejde.
Hypotese B: Interventionen vil ikke påvirke hvileblodtryk, hvilepuls og puls under søvn samt inflammationsniveau målt via koncentration af høj sensitiv C-reaktiv protein.
Hypotese C: Interventionen vil øge døgnblodtrykket.

Organisering af projektet

Projektet blev organiseret i 2 delprojekter.

Delprojekter og videnskabeligt personale

Delprojekt 1

- Undersøgelser i tre eksisterende prospektive datasæt (Copenhagen Male Study, Østerbroundersøgelsen, Den Nationale Arbejdsmiljøkohorte)
- Projektleder: Andreas Holtermann
- Videnskabelige medarbejdere:
    - fra NFA: Andreas Holtermann, Jørgen Vinsløv Hansen;
    - fra Hjerteafdelingen, Bispebjerg Hospital: Eva Prescott;
    - fra Copenhagen Male Study, Bispebjerg Hospital: Finn Gyntelberg og Poul Suadicani;
    - fra Arbejdsmedicinsk Afdeling, Køge Sygehus: Ole Steen Mortensen;
    - fra Østerbroundersøgelsen, Bispebjerg & Frederiksberg Hospital: Jacob Marott og Peter Schnohr;
    - fra Institut for Idræt og Klinisk Biomekanik, Syddansk Universitet: Karen Søgaard;
    - fra Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Berlin, Tyskland: Hermann Burr;
    - fra University of California, Los Angeles, CA, USA: Niklas Krause

Delprojekt 2

Arbejdspladsintervention blandt rengøringsassistenter i 3 virksomheder i Danmark.

- Projektleder: Mette Korshøj
- Videnskabelige medarbejdere: NFA: Andreas Holtermann, Jørgen Henrik Skotte, Mark Lidegaard, Marie Birk Jørgensen, Marie Højbjerg Ravn, Jesper Kristiansen, Hans Bay, Åse Marie Hansen (også tilknyttet Institut for Folkevidenskab, Københavns Universitet)
  Institut for Idræt og Ernæring, Københavns Universitet: Peter Krustrup
  Institut for Idræt og Klinisk Biomekanik, Syddansk Universitet: Karen Søgaard
  Hjerteafdelingen, Bispebjerg Hospital: Eva Prescott
  Arbejdsmedicinsk Afdeling, Køge Sygehus: Ole Steen Mortensen
  University of California, Los Angeles, CA, USA: Niklas Krause
  Department of Public Health, Ghent University: Els Clays

METODE

Metode for delprojekt 1

Datakilder

I dette delprojekt blev der gennemført prospektive epidemiologiske analyser baseret på følgende data:

Copenhagen Male Study

Undersøgelsen blev gennemført i 1970/1971 på ca. 5.300 mænd i alderen 40-59 år fra 14 større virksomheder i København. Undersøgelsen omfatter spørgeskemabesvarelser (sociodemografiske faktorer, livsstil, helbredsforhold, psykosociale forhold) og en række fysiologiske målinger og tests (bl.a. højde, vægt, blodtryk, Åstrands cykeltest til estimering af kondition og blodprøver). Det oprindelige formål med kohorten var at undersøge, hvordan fysisk aktivitet i arbejde og fritid og kondition influerer på risikoen for udvikling af hjertekarsygdom.

Østerbroundersøgelsen (ØBUS)

Undersøgelsen blev for første gang gennemført i 1976-1978, derefter i 1981-1983, 1991-1994, 2001-2003 og 2012-2014. Undersøgelsen omfatter af mænd og kvinder tilfældigt udvalgt fra Østerbro og Nørrebro i København. Antallet af forsøgspersoner i de forskellige runder varierer, men er ca. på 10.000-14.000 kvinder og mænd. Forsøgspersoner, der først har deltaget, bliver inviteret til at deltage i de kommende runder. Undersøgelsen omfatter spørgeskemabesvarelser (sociodemografiske faktorer, livsstil, helbredsforhold, psykosociale forhold) og en række fysiologiske målinger (bl.a. højde, vægt, blodtryk og blodprøver).

Den Nationale Arbejdsmiljøkohorte (NAK)

NAK er en repræsentativ kohorte for den danske arbejdende befolkning. NAK er blevet gennemført fra 1990 til 2010 med 5 års mellemrum. Runden i 1990 med ca. 6.000 personer blev anvendt i dette projekt. 1990-runden indbefattede telefoninterview med detaljerede spørgsmål om psykosociale og fysiske arbejdsforhold, helbred, livsstil og sociodemografiske forhold.

Fysisk aktivitet i arbejde og fritid målt med spørgeskema

Måling af fysisk aktivitet i arbejdet

Fysisk aktivitet i arbejdet blev primært målt med et spørgsmål i Copenhagen Male Study og Østerbroundersøgelsen. Spørgsmålet er udviklet af Saltin og Grimby (28). Forsøgs-personerne skulle vælge mellem følgende 4 grupper:

- Gr.1 De sidder for det meste ned og går ikke ret meget omkring på Deres arbejdsplads [lav fysisk aktivitet i arbejde]

- Gr.2 De går en hel del omkring på Deres arbejdsplads uden at skulle slæbe på tunge ting [moderat fysisk aktivitet i arbejde]

- Gr.3 De går for det meste, og De må ofte gå op at trapper og løfte forskellige ting [hård fysisk aktivitet i arbejde]

- Gr.4 De har tungt legemligt arbejde. De løfter tunge ting og anstrenger Dem fysisk [hård fysisk aktivitet i arbejde]

Besvarelserne i Gr. 3 og 4 blev slået sammen i de fleste statistiske analyser grundet få besvarelser i Gr. 4 og defineret som hård fysisk aktivitet i arbejdet.

I Den Nationale Arbejdsmiljøkohorte (NAK) blev fysisk aktivitet i arbejdet målt med fire spørgsmål: "Kræver dit arbejde at du sidder ned? (svarkategorier reverseret)", "Kræver dit arbejde fysisk anstrengelse som får dig til at puste hurtigere?", Kræver dit arbejde at du arbejder knæliggende eller hugsiddende?", og "Kræver dit arbejde at du løfter byrder der vejer mere end 20 Kg daglig?". Svarkategorierne og følgende score var: "Nærmest hele tiden" (100), "Omkring ¾ af tiden" (75), "Omkring halvdelen af tiden" (50), "Omkring ¼ af tiden" (25), "Sjælden / meget lidt" (6), "Aldrig" (0). Mænd og kvinder blev kategoriseret i 4 grupper af fysisk aktivitet i arbejdet baseret på kvartiler fra den summerede score fra alle 4 spørgsmål kalkuleret fra hele populationen.

Måling af fysisk aktivitet i fritiden

Et almindeligt anvendt spørgsmål udviklet af Saltin og Grimby (28) blev brugt til at måle fysisk aktivitet i fritiden. Forsøgspersonerne skulle vælge mellem følgende 4 grupper:

- Gr.1 De sidder som regel og læser, ser fjernsyn, går i biografen og tilbringer for det meste fritiden med stillesiddende sysler. [lav fysisk aktivitet i fritiden]

- Gr.2 De går en tur, kører lidt på cykel eller er i legemlig aktivitet i mindst 4 timer om ugen. Fx lettere havearbejde, fritidsbyggeri, bordtennis, bowling. [moderat fysisk aktivitet i fritiden]

- Gr.3 De er aktiv idrætsudøver, løber, svømmer, spiller tennis eller badminton dog i mindst 3 timer ugentlig. Udfører De hyppigt tungt havearbejde, hører De også til i denne gruppe. [høj fysisk aktivitet i fritiden]

- Gr.4 De driver konkurrenceidræt, enten svømmer eller spiller fodbold, håndbold eller løber lange distancer regelmæssigt flere gange om ugen. [høj fysisk aktivitet i fritiden]

Besvarelserne i Gr. 3 og 4 blev slået sammen i de fleste statistiske analyser grundet få besvarelser i Gr. 4 og defineret som høj fysisk aktivitet i fritiden.

Måling af kondition

Kondition (mlO_2/kg/min) blev estimeret ved en submaksimal cykeltest, hvor personens puls måles ved en given belastning (ved 100, 150 eller 200 watt afhængig af alder og vægt af forsøgsperson) efter 5 minutters cykling (29). Estimeringen af konditionen foregår med Åstrands nomogram (29). Lav kondition blev defineret som lavere end 27 mlO_2/kg/min, moderat kondition blev defineret som 27-38 mlO_2/kg/min, høj kondition blev defineret som højere end 39 mlO_2/kg/min.

Registerdata:

Nationale registre (Det Nationale Dødsårsagsregister og Det Nationale Hospitaliserings register) blev brugt for at følge forsøgspersonerne fra baselinemålingerne og fremover i tid for død af alle årsager, død fra iskæmisk hjertesygdom, generel hjertesygdom og hjerteinfarkt.

Analyser

Alle analyser blev gennemført med epidemiologiske, statistiske analysemetoder, hovedsageligt overlevelsesanalyser justeret for en række potentielle konfundere.

Metode for delprojekt 2

Design

Studiet blev gennemført som et cluster randomiseret studie med hver virksomhed indsat som en blok med dertilhørende clusters. De rengøringsassistenter, der ønskede at deltage og som mødte op til sundhedstjekket ved baseline, blev inddelt i clusters. Clusters var inddelt i strata, hver strata udgjorde de deltagere, som afrapporterede til samme mellemleder. Clusters var balanceret på følgende kriterier: Geografisk lokation af arbejdssted, køn, alder og jobanciennitet. Deltagerne blev tilfældigt udtrukket til enten en reference- eller en konditionstræningsgruppe.

Rekruttering af deltagere

Rengøringsvirksomheder i København og omegn blev rekrutteret via direkte kontakt (telefon eller email) til ledelsen. Rengøringsvirksomheder, der primært varetog rengøring på daginstitutioner, kontorer, hospitaler og skoler, blev kontaktet. Såfremt ledelsen viste interesse i studiet blev der etableret et møde mellem projektlederen på NFA og ledelsen på rengøringsvirksomheden. Ved aftale om samarbejde blev et informationsmøde for alle ansatte rengøringsassistenter planlagt i forbindelse med et personalemøde. Forud for informationsmødet blev der uddelt informationsfoldere til alle ansatte rengøringsassistenter omhandlende studiets formål, indhold og aktiviteter i forbindelse med deltagelse.

Styrkeberegninger viste, at den forventede øgning i kondition på 4 % ville kunne detekteres med et signifikansniveau på 0,05 % ved rekruttering af 52 deltagere til hver interventionsgruppe, i alt 104 deltagere. Baseret på erfaringer fra tidligere interventions-studier gennemført på rengøringsvirksomheder på Sjælland forventedes et frafald på 30 % (30). Yderligere var det forventet, at 40 % af alle adspurgte rengøringsassistenter ville tilmelde sig studiet. Derfor blev det søgt at præsentere studiet for 130 rengøringsassistenter.

Inklusionskriterierne for rengøringsvirksomheder var: At de skulle ligge i København og omegn, have mere end 50 rengøringsassistenter ansat og give de rengøringsassistenter, der ønskede deltagelse, mulighed for at deltage i betalt arbejdstid.

Inklusionskriterier for deltagere var: Ansættelse som rengøringsassistent i mere end 20 timer/uge i en af de deltagende virksomheder, være mellem 18 og 65 år gammel, ikke være gravid og underskrive et informeret samtykke om deltagelse. Eksklusionskriterier for deltagere til konditionstesten var: Hjertesvigt, hospitalsindlæggelse for hjertekar-sygdom inden for de seneste to år, hvileblodtryk ≥ 160/ ≥ 100 mmHg, smerte udløst af anstrengelse i brystregionen, kroniske lidelser, trauma, hyppig migræne og/ eller feber. Yderligere blev deltagere med plasterallergi ekskluderet fra døgnmålingerne.

Intervention

Interventionsaktiviteterne blev udviklet i tæt samarbejde mellem projektgruppen på NFA og den enkelte deltagende virksomhed via 'intervention mapping'. 'Intervention mapping' faciliterer indflydelse og høring af alle relevante interessenter (deltagende rengøringsassistenter, ledelse på rengøringsvirksomhed, fagforbund, forskere og instruktører fra NFA). Interventionsaktiviteterne skulle være motiverende og imødekomme deltagernes ønsker samt være gennemførbare på eller i nærhed af deltagernes arbejdssted. For konditionstræningsgruppen var der af forskerne nedsat en ramme for, at konditionstræningen skulle kunne gennemføres med en gennemsnitlig intensitet på 60 % af den maksimale iltoptagelse i 2x30 min/uge.

Referencegruppen blev tilbudt foredrag omhandlende sund adfærd uden henvisning til fysisk aktivitet. Foredragene var af 2 timers varighed og fandt sted hver anden måned gennem projektets 12 måneders varighed. Forslag til foredragsemner blev givet af arbejdsgruppen i 'intervention mapping' udviklingen. Deltagerne i referencegruppen blev opfordret til at komme med ideer til andre emner samt adspurgt om prioritering af foreslåede emner.

Konditionstræningsgruppen blev tilbudt 2x30 min. konditionstræning med fuld supervision i de første 4 måneder samt gradvis faldende supervision i de afsluttende 6 måneder. Forslag til aktivitet, tid på dagen, ugedag og lokation blev udviklet af arbejdsgruppen i 'intervention mapping' udviklingen. Deltagerne i konditions-træningsgruppen blev løbende adspurgt om feedback og justeringer af den tilbudte konditionstræning.

Dataindsamling

Dataindsamlingen bestod af et screeningsspørgeskema, der blev uddelt til alle ansatte rengøringsassistenter i forbindelse med informationsmødet. Tre sundhedstjek blev gennemført af instruktører blindet til randomiseringen. Der blev gennemført et sundhedstjek ved baseline, et 4 måneder efter baseline og et 12 måneder efter baseline. Ved de tre sundhedstjek blev der gennemført et spørgeskemabaseret interview, taget et hvileblodtryk og en blodprøve. Efter hvert sundhedstjek fik deltagerne feedback på den målte højde, vægt, BMI, fedtprocent, talje- og hofteomkreds og kondition samt nogle af biomarkørerne målt ved blodprøven. Såfremt nogle af de målte værdier gav anledning til bekymring, blev deltagerne opfordret til at tage kontakt til egen læge.

I tillæg blev der ved hvert sundhedstjek påsat døgnmålingsudstyr til måling af blodtryk i 24 timer (Spacelabs 90217) samt fysisk aktivitet, kropsposition (ActiGraph GT3X+) og puls (Actiheart) i 4 døgn.

Spacelabs 90217 (www.spacelabshealthcare.com) er valideret til måling af døgnblodtryk i felt (31). Døgnblodtrykket måles ved hjælp af oscillometri, og derfor bliver deltagerne bedt om at forholde sig tavse under målingen, ligesom armen skal holdes i ro. Manchetten til spacelabs 90217 blev monteret på den ikke-dominante overarm og loggren i et elastikbælte om taljen. Da spacelabs 90217 ikke er vandtæt, blev deltagerne bedt om at tage monitoren af i forbindelse med bad.

Actigraph (www.theactigraphcorp.com) er valideret til måling af fysisk aktivitet og kropsposition i felt (32, 33). Fire Actigraph-monitorer blev fæstet direkte på huden ved hjælp af plaster (3 M, Hair-Set, dobbeltklæbende tape og Fixomull, BSN medical), en på højre lår midt mellem den øvre del af knæskallen og hoftefremspringet, en lige under hoftekammen på højre side, en på den dominante overarm 3 cm under deltoideus-tilhæftningen og en på den øvre del af ryggen i højde med hvirvel T1-T2 (32).

Actiheart (www.camntech.com) er valideret til måling af puls i felt (34, 35). Pulsen måles via R-toppene i en ekko-kardiografimåling. Actiheart-monitoren var fæstet direkte på huden ved hjælp af ag-ag-cl elektroder (Ambu blue-sensor VL-00-S/25) placeret på manubrium af sternum med vandret wire eller på apex af sternum med vandret wire (36).

Alle døgnmålinger blev ved hjælp af en dagbog udfyldt af deltageren og inddelt i tid under arbejde, fritid og søvn samt tid uden døgnmålingsudstyr.

Yderligere blev der hver fjerde uge indsamlet puls under konditionstræningen på de tilstedeværende deltagere. Alle projektaktiviteter blev gennemført i betalt arbejdstid på eller i umiddelbar nærhed af arbejdsstedet for deltagerne.

Data

Det primære udfaldsmål i delprojekt 2 var kondition (mlO_2/min/kg). De sekundære udfaldsmål var pulsbelastning under arbejde, målt via døgnmålingerne under arbejde; hvilepuls, målt under blodtrykstagning ved sundhedstjek; puls under søvn, målt via døgnmålingerne under søvn; koncentration af høj sensitiv C-reaktiv protein, målt i blodprøve; og døgnblodtryk, målt via døgnmålingerne henover 24 timer. Pulsbelastning under arbejde blev beregnet som pulsreserve (forskellen mellem den estimerede maksimale puls (37) og den målte puls under søvn, defineret som den 10. laveste puls under søvn (36)). Procent af pulsreserven er på gruppeniveau ens med procent af maksimal iltoptagelse.

Data fra døgnmålingerne gennemgik et kvalitetstjek inden analyse. Pulsdata blev lukket ind i analysen, hvis den enkelte deltagers pulsdata ikke indeholdt mere end 50 % fejlmålinger. Døgnblodtryksmålinger blev lukket ind i analysen, hvis den enkelte deltager havde gennemført mere end 25 % af alle planlagte døgnblodtryksmålinger særskilt i arbejde, fritid og søvn (38).

Etnicitet er opgjort som vestlig/ikke vestlig, hvor vestlig defineres som alle europæiske lande, Australien, Canada og USA.

Hvileblodtrykket er opgjort som gennemsnittet af den anden og tredje måling ved sundhedstjekket.

Analyser

Data er analyseret i henhold til intention-to-treat-princippet, hvor alle randomiserede deltagere er inkluderet i analysen (39) ved hjælp af justerede 2x2 mixed models. Uafhængige kategoriske variable var: interventionsgruppe (reference og konditions-træning), tid (baseline, 4 måneder efter baseline og 12 måneder efter baseline) og interaktionen mellem interventionsgruppe og tid. I modellen blev deltagerne indsat som en tilfældig effekt indlejret i clusters. Dermed blev der taget højde for den clusterbaserede randomisering. Manglende observationer blev ikke imputerede (39). Konfundere er udvalgt på baggrund af tidligere litteratur og eventuelle forskelle mellem interventionsgrupperne ved baseline.

Analyserne af effekt på kondition, hvilepuls, puls under søvn og hvileblodtryk er justeret for: Baselineværdi af den givne variabel, alder, køn, dagligt indtag af medicin mod forhøjet blodtryk og/eller hjertekarsygdom, rygning og niveau af fysisk aktivitet i fritiden (for effekt på kondition) eller kondition ved baseline (for effekt på hvilepuls, puls under søvn og hvileblodtryk). Analyserne for effekt på døgnblodtryk er justeret for: Baselineværdi af døgnblodtryk, alder, køn, dagligt indtag af medicin mod forhøjet blodtryk og/eller hjertekarsygdom, rygning og kondition ved baseline. Analyserne for effekt på høj sensitiv C-reaktiv protein er justeret for: Baselinekoncentration af høj sensitiv C-reaktiv protein, alder, køn, BMI, dagligt indtag af medicin mod forhøjet kolesterol og/eller hormonbehandling, rygning, alkoholindtag og niveau af fysisk aktivitet i fritiden.

RESULTATER

I dette afsnit præsenteres hovedresultaterne fra de videnskabelige artikler, der undersøger de primære hypoteser i de to delprojekter i projektet.

Delprojekt 1

Øger hård fysisk aktivitet i arbejdet risikoen for hjertekarsygdom og dødelighed?

Overlevelsesanalyser i de tre kohorter (Copenhagen Male Study, Østerbroundersøgelsen og Den Nationale Arbejdsmiljøkohorte) viste, at mænd med hård fysisk aktivitet i arbejdet havde en forøget risiko for død af alle årsager, død fra iskæmisk hjertesygdom og generel hjertesygdom og hjerteinfarkt i forhold til mænd uden hård fysisk aktivitet i arbejdet (40-42).

Overlevelsesanalyser i Østerbroundersøgelsen og Den Nationale Arbejdsmiljøkohorte viste, at kvinder med hård fysisk aktivitet i arbejdet ikke synes at have en forøget risiko for død af alle årsager, død fra iskæmisk hjertesygdom og generel hjertesygdom og hjerteinfarkt i forhold til kvinder uden hård fysisk aktivitet i arbejdet (41, 42). Den Nationale Arbejdsmiljøkohorte viste tendenser til en u-formet association mellem grad af fysisk aktivitet i arbejdet og dødelighed for kvinder, hvor kvinder med moderat fysisk aktivitet i arbejdet havde lavest risiko, mens risikoen tenderede til at være forøget for kvinder med lav og hård fysisk aktivitet i arbejdet. Dette var dog ikke statistisk signifikant.

Reducerer høj fysisk aktivitet i fritiden den forøgede risiko for hjertekarsygdom og dødelighed fra hård fysisk aktivitet i arbejde?

Undersøgelserne i Copenhagen Male Study og Østerbroundersøgelsen viste, at høj fysisk aktivitet i fritiden generelt halverer risikoen for at dø af iskæmisk hjertekarsygdom. Derudover viste de, at moderat og/eller høj fysisk aktivitet i fritiden reducerede risikoen for død af alle årsager, død fra iskæmisk hjertesygdom og generel hjertesygdom og hjerteinfarkt blandt både mænd og kvinder med lav, moderat og hård fysisk aktivitet i arbejdet (42-44). Det blev estimeret i Østerbroundersøgelsen, at personer med moderat fysisk aktivitet i fritiden har en forventet forøget levetid med 1,5 - 3,6 år, og at personer med høj fysisk aktivitet i fritiden har en forventet forøget levetid med 2,6 - 4,7 år sammenlignet med personer med lav fysisk aktivitet i fritiden (44).

Reducerer høj kondition den forøgede risiko for hjertekarsygdom og dødelighed fra hård fysisk aktivitet i arbejdet?

Overlevelsesanalyser blandt de ca. 5.000 midaldrende mænd i Copenhagen Male Study, der fik målt konditionen i 1970/1971, viste, at mænd med et kondital højere end 39 ml O_2/kg/min – i forhold til mænd med lav kondition (kondital lavere end 27 ml O_2/kg/min) - har en halveret risiko for at dø tidligt af iskæmisk hjertekarsygdom og 40 % reduceret risiko for død af alle årsager (40, 43, 45, 46).

Vi fandt også, at mænd med høj fysisk aktivitet i arbejdet ikke havde en bedre kondition sammenlignet med mænd med lav fysisk aktivitet i arbejdet (22). Derimod er der en tydelig cross-sectionel sammenhæng mellem fysisk aktivitet i fritiden og kondition. Det er vigtigt at påpege, at målingerne af fysisk aktivitet i arbejde og fritid samt kondition er gennemført på samme tidspunkt (1970/1971), så man kan ikke konkludere, at der er en årsagssammenhæng mellem fysisk aktivitet i arbejdet i forhold til fysisk aktivitet i fritid og kondition.

Derudover fandt vi, at blandt mænd med lav kondition, havde mænd med hård fysisk aktivitet i arbejde en betydelig forøget risiko for at dø tidligt af iskæmisk hjertekar-sygdom sammenlignet med mænd med lav fysisk aktivitet i arbejde. Blandt mænd med høj kondition, har de med hård fysisk aktivitet i arbejde derimod ikke en forhøjet risiko for at dø tidligt af iskæmisk hjertekarsygdom sammenlignet med mænd med lav fysisk aktivitet i arbejde. Disse resultater blev også genfundet, når analyserne udelukkende blev lavet på mænd tilhørende lavere sociale klasser (social klasse 4 og 5) (46), som understøtter, at resultaterne ikke kan forklares af socioøkonomisk konfounding.

Delprojekt 2

Delprojekt 2 viste, at en arbejdspladsintervention med konditionstræning blandt rengøringsassistenter medførte en række positive effekter, der bidrager til at sænke risikoen for hjertekarsygdom, samt en negativ effekt, der bidrager til at øge risikoen for hjertekarsygdom (47). Derfor tyder det på, at en arbejdspladsintervention, bestående af 2x30 minutters konditionstræning om ugen i arbejdstiden blandt rengøringsassistenter, har en generel positiv effekt på sundheden i hjertekarsystemet.

Døgnmålingerne ved baseline viste, at over halvdelen (51 %) af deltagerne havde en pulsbelastning under arbejde over de anbefalede på 30 % af pulsreserven (26). Dette indikerer, at der er et behov for interventioner målrettet reduktion af pulsbelastning under arbejde, særligt blandt jobgrupper med høj risiko for at få en hjertekarsygdom.

Øges konditionen og sænkes pulsen og den relative arbejdsbelastning?

Konditionstræningen medførte signifikant øget kondition for deltagere i konditionstræningsgruppen sammenlignet med deltagere i referencegruppen. Både 4 (48) og 12 måneder efter baseline var konditionen øget med 9 %, hvilket anslås til at sænke risikoen for hjertekarsygdom med 9 % (49). Denne stigning i kondition antages at kunne relateres til det signifikante fald i såvel hvilepuls på 3,8 slag/min (5 %) som puls under søvn også på 3,8 slag/min (8 %) 4 måneder efter baseline (50). På trods af, at konditionen er øget 12 måneder efter baseline, ses der kun en signifikant effekt på hvilepuls, der er sænket med 5,3 slag/min (7 %) og ingen effekt på puls under søvn efter 12 måneder. Disse fald i hvilepuls og puls under søvn anslås til at sænke risikoen for hjertekarsygdom med 6 % (20).

På baggrund af øgningen i konditionen kombineret med fald i puls under søvn kan et fald i pulsbelastningen under arbejde forventes under forudsætning af, at arbejdskravet er uændret (24). Pulsbelastningen under arbejde faldt 11 % (- 3,5 % af den relative pulsbelastning) 4 måneder efter baseline (51) og 7 % (- 2,2 % af den relative pulsbelastning) 12 måneder efter baseline. Sådanne fald i pulsbelastning under arbejde anslås at sænke risikoen for hjertekarsygdom med op til 7 % (10).

Ændres relaterede risikofaktorer for hjertekarsygdom?

Yderligere havde denne arbejdspladsintervention med konditionstræning også en positiv effekt på koncentrationen af høj sensitiv C-reaktiv protein (52), en biomarkør for niveauet af inflammation i hele kroppen. Sammenligninger af deltagerne i konditionstrænings- og referencegruppen viste, at 4 måneder efter baseline havde deltagerne i konditionstræningsgruppen en 37 % (- 0,54 μg/ml) lavere koncentration af høj sensitiv C-reaktiv protein i forhold til deltagerne i referencegruppen (52). Ligeledes sås, at 12 måneder efter baseline havde deltagerne i konditionstræningsgruppen en 44 % (- 0,65 μg/ml) lavere koncentration af høj sensitiv C-reaktiv protein i forhold til deltagerne i referencegruppen. Fald i koncentrationen af høj sensitiv C-reaktiv protein i dette omfang tilskrives reduktioner i risikoen for hjertekarsygdom op til 15 % (53).

Arbejdspladsinterventionen med konditionstræning havde også negative effekter ved sammenligning af deltagerne i konditionstræningsgruppen og referencegruppen. Fire måneder efter baseline sås stigninger i både hvile- og døgnblodtrykket (54, 54). Det systoliske hvileblodtryk steg med 3,6 mmHg (3 %), og der sås ingen ændringer i det diastoliske hvileblodtryk 4 måneder efter baseline (55). Døgnblodtrykket steg 4 måneder efter baseline både systolisk 3,6 mmHg (3 %) og diastolisk 2,3 mmHg (3 %) (54). Sådanne stigninger i såvel hvile- som døgnblodtryk anslås at øge risikoen for hjertekarsygdom med op til 10 % afhængig af udgangsniveauet (18). Tolv måneder efter baseline sås ingen ændringer i hverken hvile- eller døgnblodtryk, som kan skyldes frafald, og at relativt få deltagere gennemførte døgnblodtryksmålingen efter 12 måneder.

DISKUSSION

Delprojekt 1

Undersøgelserne i Copenhagen Male Study, Østerbroundersøgelsen og Den Nationale Arbejdsmiljøkohorte viste, at hård fysisk aktivitet i arbejdet synes at forøge risikoen for hjertekarsygdom og/eller dødeligheden blandt mænd. Dette fund er i henhold til øvrige nyere undersøgelser i en række andre kohorter (6, 7, 9, 10). Den øgede risiko for hjertekarsygdom og dødelighed fra hård fysisk aktivitet i arbejdet er foreslået forklaret gennem en varig overbelastning (stress) på hjertekarsystemet, som kan forårsage åreforkalkning med følgelig hjertekarsygdom og dermed førtidig dødelighed (10, 13, 14).

Dette er i modsætning til undersøgelserne i Østerbroundersøgelsen og Den Nationale Arbejdsmiljøkohorte, der viste, at kvinder med hård fysisk aktivitet i arbejdet ikke har en forøget risiko for hjertekarsygdom og dødelighed. Derimod indikerede analyserne i Den Nationale Arbejdsmiljøkohorte en tendens til en u-formet association mellem grad af fysisk aktivitet i arbejdet og dødelighed for kvinder. Der er relativt få kohorter, der har undersøgt sammenhængen mellem fysisk aktivitet i arbejdet og risiko for hjertekar-sygdom og dødelighed blandt kvinder. Resultaterne fra disse få kohorter blandt kvinder er utvetydige, da nogle studier viser en forøget risiko (7, 9), mens andre studier viser ingen (56) eller en beskyttende effekt (57) af hård fysisk aktivitet i arbejdet.

At hård fysisk aktivitet i arbejdet synes at øge risikoen for hjertekarsygdom og dødelighed blandt mænd men ikke kvinder, kan skyldes, at ”hård fysisk aktivitet i arbejdet” kan indebære flere forskellige ergonomiske eksponeringer blandt mænd end kvinder. For eksempel er det sandsynligt, at ”hård fysisk aktivitet i arbejdet” i større grad indeholder tungt og statisk løfte-og-bære-arbejde blandt mænd end kvinder, mens ”hård fysisk aktivitet i arbejdet” i større grad indeholder mere gang og dynamiske bevægelser blandt kvinder end mænd. Meget tungt og statisk løfte-og-bære-arbejde per dag er antaget at medføre et betydeligt stress på hjertekarsystemet uden at forbedre kondition og helbred, mens meget gang og dynamiske bevægelser per dag ikke forårsager et ligeledes højt stress på hjertekarsystemet (56, 58).

Undersøgelserne i Copenhagen Male Study og Østerbroundersøgelsen viste, at høj fysisk aktivitet i fritiden generelt halverer risikoen for at dø af iskæmisk hjertekarsygdom. Derudover viste de, at moderat og høj fysisk aktivitet i fritiden reducerede risikoen for død af alle årsager, død fra iskæmisk hjertesygdom, generel hjertesygdom og hjerte-infarkt blandt både mænd og kvinder stort set uafhængig af fysisk aktivitet i arbejdet. Disse fund er i tråd med nyere observationsstudier i andre kohorter, der finder, at fysisk aktivitet i fritiden beskytter mod hjertekarsygdom og førtidig dødelighed blandt personer med forskellig grad af fysisk aktivitet i arbejdet (9, 59). Samlet set indikerer disse studier, at personer med hård fysisk aktivitet i arbejdet bør anbefales at være moderat til høj fysisk aktiv i fritiden. Det vides dog ikke, hvilken type intensitet eller varighed den fysiske aktivitet i fritiden bør indeholde blandt personer med hård fysisk aktivitet i arbejdet.

Forskellen på sundhedseffekten af fysisk aktivitet i fritid og arbejde kan skyldes, at karakteristikkerne af fysisk aktivitet, der forekommer under arbejde og fritid, er forskellige. Fysisk aktivitet under arbejdet forekommer henover flere timer, mange dage i stræk, og indeholder vanligvis aktiviteter som tunge løft, skub, træk, monotont repetitivt arbejde og statiske arbejdsstillinger med begrænsede muligheder for pauser og tilstrækkelig restitution (8, 45). I kontrast forekommer fysisk aktivitet i fritiden oftest over kortere tidsperioder med dynamiske bevægelser, som øger metabolismen og pulsen til tilstrækkelig højt niveau til at øge konditionen med tilstrækkelig variation og restitution (8, 45). Disse nævnte karakteristikker af fysisk aktivitet i arbejdet er generelt anset for værende risikofaktorer for reduceret helbred, mens karakteristikkerne af fysisk aktivitet i fritiden er veldokumenteret til at forbedre helbredet.

Undersøgelsen i Copenhagen Male Study angående fysisk aktivitet i arbejdet og kondition viste, at mænd med lavt kondital og hård fysisk aktivitet i arbejdet havde en betydelig forøget risiko for at dø tidligt af iskæmisk hjertekarsygdom sammenlignet med mænd med lav fysisk aktivitet i arbejdet. Blandt mænd med høj kondition har de med hård fysisk aktivitet i arbejdet derimod ikke en forhøjet risiko for at dø tidligt af iskæmisk hjertekarsygdom sammenlignet med mænd med lav fysisk aktivitet i arbejdet.

Konditionen har over flere årtier været anset som afgørende for både at være i stand til at udføre hård fysisk aktivitet i arbejdet og for at klare belastningen helbredsmæssigt (23-25). Dette studie er derimod en af de første større prospektive undersøgelser, der dokumenterer, at en ubalance mellem fysisk aktivitet i arbejdet og konditionen medfører en forøget risiko for at dø tidligt af iskæmisk hjertekarsygdom. Resultaterne understøtter dermed ILO’s anbefaling om, at belastningen af kroppen ved hård fysisk aktivitet i arbejdet henover en arbejdsdag bør vurderes relativt i forhold til medarbejderens kondition (10, 25, 26, 60). Dette studie indikerer derfor et behov for at undersøge tiltag, der sikrer en god balance mellem fysiske krav i arbejdet og kondition. Mulige tiltag kunne være ergonomiske og/eller organisatoriske tilpasninger med henblik på reduktion af den fysiske belastning henover arbejdsdagen eller sikring af tilstrækkelig variation, restitution og hvile. Yderligere kunne fysisk træning i arbejdstiden tilbydes for at øge konditionen.

Delprojekt 2

Delprojekt 2 viste, at en arbejdspladsintervention med konditionstræning blandt rengøringsassistenter medførte primært positive effekter som øget kondition, sænket hvilepuls, puls under søvn, pulsbelastning under arbejde og koncentration af høj sensitiv C-reaktiv protein. Omvendt steg både hvile- og døgnblodtrykket 4 måneder efter baseline, hvilket er en negativ effekt siden dette vil øge risikoen for hjertekarsygdom.

De primært positive effekter er opnået efter 4 måneders superviseret konditionstræning i 2x30 min/uge med en deltagerprocent på 64. Efter yderligere 6 måneders delvist superviseret konditionstræning i 2x30 min/uge fandtes der udelukkende positive eller ingen signifikante effekter. Dette indikerer, at konditionstræning i arbejdstiden reducerer risikoen for hjertekarsygdom blandt rengøringsassistenter.

Tidligere studier har vist, at rengøringsassistenter er meget fysisk aktive i deres job, da de går eller står det meste af arbejdstiden (61, 62) med megen aktivitet med armene (aftørring, brug af mopper, skub af vogn m.m.) (62, 63). Den fysiske aktivitet under rengøringsarbejde belaster hjertekarsystemet, hvilket kan ses via den høje pulsbelastning under arbejde (61, 62), målt til gennemsnitlig 31 % af pulsreserven i dette studie. Dog er pulsbelastningen under rengøringsarbejde ikke over 60 % af pulsreserven og dermed ikke tilstrækkelig høj til at øge konditionen (61, 64, 65). Så vidt vides, er dette studie det første, der har kunnet påvise et væsentligt fald i pulsbelastningen under rengøringsarbejde. Dette fald i pulsbelastningen under rengøringsarbejde kan forklares ud fra den øgede kondition samt sænkede hvilepuls og puls under søvn, da pulsbelastningen under rengøringsarbejde er direkte afhængig af disse faktorer (24). Disse fund er af betydning, da de bidrager til en lavere risiko for hjertekarsygdom (10, 21, 49, 66).

Denne arbejdspladsintervention med konditionstræning blandt rengøringsassistenter medførte primært positive effekter, men også en negativ effekt i form af stigninger i hvile- og døgnblodtryk 4 måneder efter baseline. Efter 12 måneder sås ingen ændring i hverken hvile- eller døgnblodtryk, eventuelt på grund af frafald af deltagere og dermed færre målinger. En mulig årsag til, at blodtrykket steg, kan være, at deltagerne i konditionstræningsgruppen er blevet overbelastede, hvilket kan skyldes, at over halvdelen af deltagerne i arbejdstiden havde en pulsbelastning over det anbefalede ved baseline. For at undersøge dette nærmere blev deltagerne inddelt i, om de ved baseline havde en pulsbelastning i arbejdet på over eller under den anbefalede grænse. Sammenligninger af deltagerne i konditionstrænings- og referencegruppen viste, at de deltagere, der ved baseline havde en pulsbelastning i arbejdet under den anbefalede grænse, ikke ændrede hverken deres hvile- eller døgnblodtryk efter interventionen.

Hvorimod at deltagere, der ved baseline havde en pulsbelastning i arbejdet over den anbefalede grænse, øgede både deres hvile- og døgnblodtryk betydeligt.

Denne analyse, inddelt i pulsbelastning i arbejde over eller under den anbefalede grænse, giver anledning til at overveje, hvordan denne potentielle negative effekt på blodtrykket kan undgås blandt dem med høj pulsbelastning i arbejde. Vort bedste forslag vil være at integrere konditionstræning med ergonomiske og/eller organisatoriske tiltag for at reducere pulsbelastningen under arbejde og dermed forebygge en potentiel stigning blodtryksstigning. Dette er dog ikke undersøgt i dette projekt, men vil være relevant at afprøve i fremtidige studier.

Konklusion

Overordnet viste projektet, at hård fysisk aktivitet i arbejdet synes at forøge risikoen for hjertekarsygdom og førtidig dødelighed blandt mænd, men ikke blandt kvinder. Både høj fysisk aktivitet i fritiden og høj kondition synes at være beskyttende faktorer for hjertekarsygdom og dødelighed fra hård fysisk aktivitet i arbejdet.

Arbejdspladsinterventionen med konditionstræning blandt rengøringsassistenter viste en række positive effekter på risikofaktorer for hjertekarsygdom, såsom øget kondition, sænket pulsbelastning under arbejde, reduceret puls under hvile og søvn og sænket inflammationsniveau, dog med en stigning af blodtrykket under hvile og henover døgnet.

Samlet set understøtter projektet sammenhængen mellem hård fysisk aktivitet i arbejdet og risiko for hjertekarsygdom og dødelighed samt den beskyttende helbredseffekt af høj kondition og fysisk aktivitet i fritiden for personer med hård fysisk aktivitet i arbejdet.

Arbejdspladsinterventionen med konditionstræning gav en række positive effekter, men også en negativ helbredseffekt. For at opnå udelukkende positive helbredseffekter fra denne type sundhedsfremme blandt medarbejdere med hård fysisk aktivitet i arbejdet vil vort bedste forslag være at integrere konditionstræning med ergonomiske og/eller organisatoriske tiltag, der reducerer arbejdsbelastningen og sikrer tilstrækkelig restitution og hvile. Dette er dog ikke undersøgt i dette projekt, men behøves at afprøves i fremtidige studier.

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APPENDIKS: FORMIDLINGSAKTIVITETER

I. Formidling til brugerne

I.a Skriftlig formidling til brugerne

1) Individuel tilbagemelding til alle fremmødte deltagere ved alle sundhedstjek på samtlige deltagende virksomheder
2) Mundtlig præsentation og diskussion af resultater på virksomhedsniveau efter 4 måneders opfølgning samt efter 12 måneders opfølgning til virksomhedens ledelse, medarbejderrepræsentanter, tillidsrepræsentant samt sikkerheds- og arbejdsmiljørepræsentant.
3) Tilbagemeldingsrapport til virksomhederne med resultater på virksomhedsniveau efter 4 måneders opfølgning samt efter 12 måneders opfølgning.

I.b Oplæg til brugerne

1) Mundtlig plenumsoplæg fra projektet ved AM2010 i Nyborg i 2010
2) Mundtlig plenumsoplæg fra projektet ved Virksomhed og tovholderkonference, 3F, Februar 2012
3) Mundtlig plenumsoplæg fra projektet ved konference af Falck Healthcare, København, Maj 2012
4) Præsentation fra projektet for arbejdsmiljørådgivere fra CRECEA, Maj 2012
5) Mundtligt oplæg omhandlende projektet ved TDC i København og Århus, Maj 2013
6) Formidlingsmøde omhandlende projektet på NFA, Oktober 2013
7) Mundtligt oplæg og seminar omhandlende interventionsprojektet ved AM2013 i Nyborg, November 2013
8) Mundtlig plenumsoplæg fra projektet ved AMFF årskonference, København, Januar 2014
9) Mundtlig oplæg omhandlende projektet ved Munch asfalt i Nyborg, Januar 2014
10) Mundtlig præsentation fra projektet ved AM2014 i Nyborg, November 2014
11) Mundtlig plenumsoplæg fra projektet ved AMFF årskonference, København, Januar 2015

II. Formidling til forskere

II.a. Artikler, publiceret i peer-reviewede videnskabelige tidsskrifter

1) Holtermann A. Occupational and leisure-time physical activity and coronary heart disease. Occupational Environmental Medicine. May 2015. Online First
2) Holtermann A, Marott JL, Gyntelberg F, Søgaard K, Mortensen OS, Prescott E, Schnohr P. Self-reported cardiorespiratory fitness: prediction and classification of risk of cardiovascular disease mortality and longevity-a prospective investigation in the copenhagen city heart study. J Am Heart Assoc. 2015 Jan 27;4(1). pii: e001495.
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II.b. Kommende artikler, under evaluering i peer-reviewede videnskabelige tidsskrifter

1) Korshøj M. Krause N. Clays E. Søgaard K. Krustrup P. Holtermann A. Does aerobic exercise increase 24-hour ambulatory blood pressure among workers with high occupational physical activity? – A randomized controlled trial.
2) Korshøj M. Højbjerg MR. Holtermann A. Hansen ÅM. Krustrup P. Aerobic exercises reduce biomarkers related to cardiovascular risk among cleaners. – Effects of a worksite intervention RCT.
3) Korshøj M. Clays E. Lidegaard M. Skotte JH. Holtermann A. Søgaard K. Krustrup P. Is aerobic workload positively related to ambulatory blood pressure? – A cross sectional field study among cleaners.
4) Korshøj M. Lidegaard M. Skotte JH. Krustrup P. Jørgensen MB. Søgaard K. Holtermann A. Long term effects on risk factors for cardiovascular disease after 12 months of aerobic exercise intervention. – A worksite RCT among cleaners.

II.c. Præsentationer ved videnskabelige konferencer med publicerede peer-reviewede abstracts

Abstracts

1) Inviteret keynote forelæsning fra projektet og abstrakt ved den internationale PREMUS konference i Busan, Syd-Korea, Juli 2013
2) Inviteret keynote forelæsning fra projektet og abstrakt ved den Tyske Sportsmedicinske årskonference, Frankfurt, Tyskland, September 2014
3) Inviteret keynote forelæsning fra projektet ved den Brasilianske Ergonomikonference ved Sao Carlos, Brasilien, September 2014

4) Abstract og mundtlig præsentation fra projektet ved den internationale ICOH konference i Cancun, Mexico, Marts, 2012.
5) Abstract og mundtlig præsentation fra projektet ved den internationale EPICOH konference i 2011 i Oxford, England
6) Abstract og mundtlig præsentation fra projektet ved den internationale ICOH-CVD konference i Marts 2013 i Tokyo, Japan
7) Abstract og mundtlig præsentation fra projektet ved den internationale ODAM-NES konference i August 2014 i København, Danmark

II.d. Præsentationer for forskere.

1) Mundtlig præsentation fra projektet på NFA i København, December 2009
2) Mundtlig præsentation fra projektet ved BAuA (Det tyske arbejdsmiljøinstitut i Berlin), Januar 2011
3) Mundtlig præsentation fra projektet ved Arbejdsmedicinsk Klinik Århus, Januar 2011
4) Mundtlig præsentation fra projektet ved Arbejdsmedicinsk Klinik Bispebjerg, Februar 2011
5) Mundtlig præsentation fra projektet ved Norges Teknisk Videnskabelige Universitet, Trondheim, Norge, Maj 2011
6) Mundtlig præsentation fra projektet ved Vrije Universitet, Amsterdam, Holland, November 2011
7) Undervisning fra projektet ved PhD kursus i fysisk aktivitet og helbred ved SDU, Odense, Maj 2012
8) Mundtlig præsentation fra projektet ved FIOH, Helsinki, Finland, Oktober 2012
9) Mundtlig præsentation fra projektet ved årsmødet i Østerbroundersøgelsen, Frederiksberg Hospital, Marts 2013
10) Mundtlig præsentation fra projektet ved Svensk Arbejdsmedicinsk vårmøde, Malmø, Sverige, April 2013
11) Mundtlig præsentation fra projektet ved Nordisk seminar om objektive felt målinger af fysisk aktivitet, siddetid og arbejdseksponering ved NFA, København, Juni 2013
12) Mundtlig præsentation fra projektet ved Universitetet i Gävle, Sverige, September 2013
13) Mundtlig præsentation fra projektet ved Stressforskningsinstituttet i Stockholm, Sverige, Januar 2014
14) Undervisning fra projektet for specialestuderende ved Idræt ved Københavns Universitet, Februar 2014
15) Mundtlig plenumsoplæg fra projektet ved Center for forebyggelse, Glostrup Hospital, København, Marts 2015

III. Afhandlinger

III.a Ph.d.-afhandlinger

1) Korshøj M. Physical work demands and fitness. – Effects on risk factors for cardiovascular disease from a randomized controlled trial among cleaners. Institut for Idræt og Ernæring, Natur- og biovidenskabelige Fakultet, Københavns Universitet.

III.b Specialeafhandlinger

1) Ravn MH. Fysisk aktivitet og risiko for hjertekarsygdom blandt kvindelige rengøringsassistenter. Institut for Idræt og Ernæring, Natur- og biovidenskabelige Fakultet, Københavns Universitet.
2) Pedersen KMK. Nørgaard LM. The acute and long-term effect of aerobic training on ambulatory blood pressure in cleaners. Sport Science and Clinical Biomechanics, Sports and Health University of Southern Denmark.
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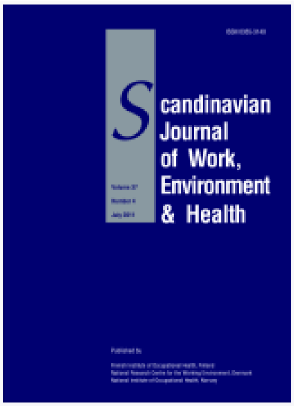
POPULÆRVIDENSKABELIG FORMIDLING, LINKS OG ARTIKLER FRA PROJEKTET

Hjemmeside

http://www.arbejdsmiljoforskning.dk/da/projekter/fysiske-arbejdskrav-og-fitness-betydning-for-hjertekarsygdom/publikationer

Artikler

Holtermann A, Mortensen OS, Burr H, Søgaard K, Gyntelberg F, Suadicani P. Arbejdskrav, fysisk aktivitet i fritiden og kondital. Miljø og sundhed, 2010;3: 3-10



Original article

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Does aerobic exercise improve or impair cardiorespiratory fitness and health among cleaners? A cluster randomized controlled trial

by Korshøj M, Lidegaard M, Skotte JH, Krustrup P, Krause N, Søgaard K, Holtermann A

A worksite aerobic exercise intervention among cleaners seems to improve cardiorespiratory fitness, aerobic workload, resting and sleeping heart rate but increases systolic blood pressure. Aerobic exercise seems to induce extensive positive cardiovascular effects, but recommendations of aerobic exercise should account for the potential cardiovascular overload of workers with high occupational physical activity and low cardiorespiratory fitness.

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Key terms: Actiheart; aerobic exercise; aerobic training; aerobic workload; blood pressure; cardiorespiratory fitness; cleaner; cluster randomized controlled trial; Denmark; physical activity; physical work demand; RCT; resting heart rate; sleeping heart rate; step test; work demand; worksite intervention

*O*riginal article

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Does aerobic exercise improve or impair cardiorespiratory fitness and health among cleaners? A cluster randomized controlled trial

by Mette Korshøj, MSc,[1,2] Mark Lidegaard, MSc,[1] Jørgen H Skotte, MS,[1] Peter Krustrup, PhD,[2,3] Niklas Krause, PhD,[4] Karen Søgaard, PhD,[5] Andreas Holtermann, PhD [1,5]

Korshøj M, Lidegaard M, Skotte JH, Krustrup 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* – online first. doi:10.5271/sjweh.3475

Objective It is unknown if aerobic exercise overloads or improves the cardiovascular system among workers with high occupational physical activity. This was investigated in a worksite randomized controlled trial (RCT) of aerobic exercise among cleaners.

Methods We randomized 116 cleaners between 18–65 years. The aerobic exercise group (N=57) performed worksite aerobic exercise (30 minutes twice a week) and the reference group (N=59) received lectures. Cardiorespiratory fitness, blood pressure (BP) and diurnal heart rate (HR) for measuring aerobic workload [% HR reserve (% HRR)] were collected at baseline and after four months. A repeated measure 2×2 multi-adjusted mixed-model design was applied to compare the between-group differences in an intention-to-treat analysis.

Results Between-group differences (P<0.01) were found: cardiorespiratory fitness 2.2 [standard error (SE) 0.8] ml $O_2 \times min^{-1} \times kg^{-1}$ [95% confidence interval (95% CI) 0.6–3.8], aerobic workload - 3.5 (SE 1.2) % HRR (95% CI - 5.9– -1.0), resting HR -3.8 (SE 1.2) bpm (95 % CI -6.1– - 1.4), sleeping HR -3.8 (SE 1.1) bpm (95% CI - 5.9– - 1.7), and systolic BP 3.6 (SE 1.3) mmHg (95% CI 1.1–6.0).

Conclusions Worksite aerobic exercise seems to improve cardiorespiratory fitness, aerobic workload, and resting and sleeping HR, but increase systolic BP among cleaners. Beneficial physiological cardiovascular effects are seen from aerobic exercise, but also a harmful effect is evident. Therefore, recommendations should take into consideration the potential cardiovascular overload from additional aerobic exercise on workers with high levels of occupational physical activity.

Key terms Actiheart, aerobic training, aerobic workload, blood pressure, Denmark, physical activity, physical work demand, RCT, resting heart rate, sleeping heart rate, step test, work demand, worksite intervention

A recent meta-analysis (1) reports that moderate and high levels of occupational physical activity increase the risk of cardiovascular disease (CVD). The risk for CVD is especially strong among workers who have high levels of occupational physical activity combined with low cardiorespiratory fitness (2, 3). Compared to a worker with high cardiorespiratory fitness, workers with low cardiorespiratory fitness experience a higher relative aerobic workload when performing the same physical work task (4). Long-term high relative aerobic workload can cause harmful arterial wall stress (5) causing atherosclerosis (6). Therefore, a balanced relationship between occupational physical activity and cardiorespiratory fitness of the worker is recommended for reducing overall risk of work-related cardiovascular overstrain (7–9). Specifically, the International Labour Organization has recommended that the average aerobic workload should not exceed 30% during an 8-hour working day (10, 11).

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Heart rate reserve (HRR) is a validated objective measure of relative aerobic workload, ie, the relationship between physical work demands and a worker's aerobic capacity (cardiorespiratory fitness) (12, 13). HRR is assessed by resting heart rate, which depends on cardiorespiratory fitness, and maximal heart rate (HR_{max}), which depends on age (14), and is thereby applicable across workers of varying age and aerobic capacities (15).

An imbalance between physical work demands and cardiorespiratory fitness can be targeted either by reducing physical work demands or enhancing cardiorespiratory fitness (3, 9) or the combination thereof. To our knowledge, a reduction of the relative aerobic workload by aerobic exercise has not yet been shown to be successful among blue-collar workers. High quality aerobic exercise interventions among workers with high levels of occupational physical activity are few and with conflicting findings (16–19), especially regarding cardiovascular risk factors such as cardiorespiratory fitness and blood pressure (BP) (20, 21).

Actually, it has been discussed in the literature, whether introducing aerobic exercise could overload and thereby impair the cardiovascular system among workers with high levels of occupational physical activity (22, 23). Workers with high levels of occupational physical activity often have a low cardiorespiratory fitness (4, 24–26) and limited ability for pauses and restitution, which may result in an increased risk of overloading and impairing the cardiovascular system (22). Thus, an aerobic exercise intervention may affect factors for cardiovascular disease both positively and negatively. Clearly, it is important to investigate if aerobic exercise among workers with high occupational physical activity will reduce their cardiovascular risk.

Cleaning is characterized by high levels of occupational physical activity (24, 27, 28). Cleaners' cardiorespiratory fitness has been described as relatively low, and consequently a high relative aerobic workload is expected (4, 28). Moreover, a high prevalence of other cardiovascular risk factors including hypertension and obesity (25, 29), and an overall elevated CVD risk have been reported among cleaners (30, 31). Classical interventions have aimed to lower the relative aerobic workload among cleaners through the ergonomic improvement of tools (32–34). Additionally, a natural experiment has been used to evaluate work technique and organizational aspects in relation to relative aerobic workload (28). However, these studies did not find significant reductions in the relative aerobic workload by intervening on the physical work demands with ergonomic or organizational interventions. An alternative approach to decrease the aerobic workload is an intervention aimed at enhancing the cardiorespiratory fitness with aerobic exercise. Cleaners therefore constitute a suitable study population to investigate if worksite aerobic exercise will improve cardiorespiratory fitness, relative aerobic workload and cardiovascular risk factors among workers with high occupational physical activity.

The main objective of this study was to investigate if a worksite aerobic exercise intervention will improve cardiorespiratory fitness, relative aerobic workload, and other cardiovascular risk factors in a cluster randomized controlled trial (RCT) among cleaners. The main hypotheses of the study were that the worksite aerobic exercise intervention would (i) increase the cardiorespiratory fitness, (ii) decrease the aerobic workload, and (iii) not modify BP or resting and sleeping heart rate (testing the null hypothesis).

Methods

Study design

As part of a cluster RCT, the intervention was divided into two phases with different aims. The aim of phase one, from baseline to 4-months follow-up, was to evaluate the efficacy of the intervention on cardiorespiratory fitness, aerobic workload, and cardiovascular risk factors. Outcomes were measured at baseline, and again at 4 and 12 months after baseline (35). The present paper reports the results from the first intervention phase (0–4 months) on cardiorespiratory fitness and cardiovascular risk factors.

The Danish Data Protection Agency and the Ethics Committee for the regional capital in Denmark (journal number H-2-2011-116) approved the study, which was conducted in accordance with the Helsinki Declaration and is registered as ISRCTN86682076 in the Current Controlled Trials (www.controlled-trials.com/ISRCTN86682076).

Recruitment of worksites and study participants

Cleaning companies in the suburban area of Copenhagen, Denmark, were recruited via direct phone or email contact to the management. If the company expressed an interest in the project, a meeting was arranged between the research group and company management. If the company agreed to participate, written information about the aim, content and activities involved in participation (project activities) was distributed to all employed cleaners, and they were also invited to an information meeting. Employed cleaners completed a screening questionnaire, collecting background information such as ethnicity, smoking status, job seniority, and levels of physical activity during working hours and leisure time (35). Additionally, the cleaners were asked if they wished to participate in the study, and if not, the reason why.

At company level, study inclusion criteria were staff of >50 employed cleaners and management's permission for cleaners to participate in the project activities during paid working time. At participant level, inclusion criteria were age 18–65 years, employment as cleaning assistant for >20 hours per week, and signed informed consent to participate in the study.

The only exclusion criterion for participating in the intervention was pregnancy. However, the following conditions excluded participation in the specific physical capacity tests: congestive heart failure, hospital admission for myocardial infarction or acute coronary syndrome within the last two years, angina pectoris, severe hypertension (≥160/≥100 mmHg), serious or chronic illness, severe trauma, frequent migraine, and fever on the day of testing. Allergy to adhesive plasters excluded participation in diurnal HR measurements.

Randomization

Randomization was performed at cluster level. A cluster was set within strata, and stratums were formed according to which manager the participant reported. Clusters were balanced on geographical work location, gender, age, and job seniority. To minimize imbalance across several strata, the clusters were paired according to number of participants, gender, age, and job seniority, within each stratum. A stratum was named alphabetically, and a cluster was named consecutively within each stratum. The randomization was carried out by a researcher blinded to the identity of the participants, strata, and clusters. Three researchers supervised the reliability of the randomization procedure. All paired clusters assigned to the specific stratum were drawn from an opaque, tossed bag and were alternately allocated to either reference or aerobic exercise group, depending on the flip of a coin. Tails decided allocation of the first of the two drawn paired clusters to the reference group and heads to the aerobic exercise group. The second of the two drawn paired clusters was allocated to the group opposite to the first (35).

Intervention

During the intervention, the reference group was offered two lectures of two hours each. The aerobic exercise group was offered supervised aerobic exercise of 2×30 minutes/week, in total 32 sessions. All project activities were carried out during paid working hours, at or nearby the worksite. The lectures addressed healthy living, but not physical activity, and participants were invited to suggest topics. The aerobic exercise was aimed to be performed at an intensity of ≥60% of maximal oxygen consumption (VO_{2max}) for enhancing the cardiorespiratory fitness (36). Through a modified intervention mapping approach (37), the aerobic exercises were tailored to each of the enrolled companies individually (35). The following two key points determined the intervention protocol: (i) Feasibility: it should be possible to execute the aerobic exercise at or nearby the enrolled company, during paid working hours; (ii) Motivation: the intervention activities should apply to the participants' preferences. In order to meet these requirements, company-specific intervention protocols were developed in collaboration between researchers and representatives from the company management, employed cleaners, and union.

Data collection

All participants were tested at baseline and after the 4-months intervention period. The test consisted of a structured interview, physical testing of health- and capacity-related measures and objective diurnal measures of HR (35). Participants got instant feedback from the physical testing. Participants were encouraged to contact a physician if their systolic or diastolic BP exceeded recommended levels (≥140 and/or ≥90 mmHg) (38). HR was measured over four days (mostly two working and two non-working days). Participants were instructed in how to wear the monitor and to write a log of working hours, sleeping and waking time, and time periods spent without monitors. During the diurnal measurements, participants were asked to live their normal every-day life.

The interview assessed sex, education, occupational group, employment status, job seniority, level of perceived exertion during work on a 6–20 scale (39), occupational and leisure-time physical activity (40), general health (41), diagnosed illnesses, and daily use of heart disease or anti-hypertension medication. The interview approach was chosen with the aim of collecting background data without missing observations because many of the participants are not ethnic Danes and have poor reading and writing skills.

Physical examinations measured body weight (kg) and fat (%) with a bioelectric-impedance-analysis tool, Tanita BC418, (Tanita Corp, Toyko, Japan), height with Seca model 213 1721009, and waist circumference with Seca model 201 (Seca, Hamburg, Germany). The waist was defined as the narrowest point between the lowest rib and the iliac crest (42, 43). Body mass index (BMI), was calculated as body weight (kg) divided by body height squared (m^2) (42). Three BP measurements were collected with Omron M6 Comfort (Omrom Healthcare, Kyoto, Japan) on the upper-left arm after minimum 15 minutes of sitting rest. Level of cardiorespiratory fitness was estimated by a sub-maximal step test (44) conducted on a bench of 30 cm height for females and 35 cm for males. Step frequency was increased from 0.2 steps per second to maximal 0.8 steps per second, at maximal six minutes of testing time. The step test was terminated when the participant could no longer keep the stepping rhythm or properly extend the knee. Measurements were conducted with participants wearing light clothes and no shoes.

The diurnal measurements of HR were performed with Actiheart (Camntech, Cambridge, UK). Actiheart is validated for measurement of HR, HR variability, and estimation of energy expenditure in the field (45, 46). The electrocardiographic raw signals are measured with a sensitivity of 0.25 mV, and HR is calculated as the number of R peaks in the QRS complex per minute. Before measurement, the Actiheart monitor was initialized by gender and age, and mounted with ag-ag-cl pre-gelled electrodes (Ambu blue sensor VL-00-S/25, Ambu Ballerup, Denmark) at one of the validated body positions (47).

During the intervention period, the instructor registered participation in the aerobic exercise group at every session. Additionally, Actiheart was used to measure the intensity of the aerobic exercise every fourth week at one session, which was calculated in percent of HRR (48). HRR was defined as the difference between the estimated HR_{max} (14) and the sleeping HR (SHR), with SHR defined as the 10^{th} lowest recorded HR value during 24 hours (49). HRR represents the workers relative aerobic workload as the range between SHR and HR_{max} (48). HRR is based on measured HR throughout the 24-hour measurements, and reflects both physical and psychosocial demands (50).

Sample size

The power calculation, performed prior to the study, showed that the expected increase in cardiorespiratory fitness of 4% would take 52 participants in each of the two intervention groups to show significance at a level of 0.05. Sample size calculations assumed recruitment of 40% of eligible cleaners and a dropout rate of 30% during the intervention (35).

Statistical analysis

The primary outcome of this trial is 4-months change in cardiorespiratory fitness (ml $O_2 \times min^{-1} \times kg^{-1}$). Secondary outcomes are 4-months changes in relative aerobic workload (% HRR), RHR in beats-per-minute (bpm), SHR (bpm), and resting systolic BP (mmHg). Only HR measurements with beat error of ≤50% were included to meet the data quality criteria set by Skotte and colleagues (51).

Ethnicity was classified as western or non-western based on country of birth. All European countries, Australia, Canada, and USA were considered western. The mean of the second and third BP measurement was calculated and evaluated as a secondary outcome.

Statistical analysis

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

All analyses were performed according to the intention-to-treat principle, in which all randomized participants are included in the statistical analyses (52). Missing values were imputed for neither outcome nor covariate variables (53). Both within- and between-group 4-month changes of all outcomes were computed with standard errors (SE) and 95% confidence intervals (95% CI). Differences in 4-month changes of all outcomes were analyzed in repeated-measures 2×2 mixed -model design. Independent categorical variables (fixed factors) were group (aerobic exercise and reference), measurement time (baseline and 4-month follow-up), and the interaction between group and measurement time. Participants were entered in the model as a random effect nested in clusters to account for the cluster-based randomization. Covariates were chosen based on: baseline differences between groups, theoretically considered confounders, and their statistical association with the group and measurement time. The following covariates (reference value in parenthesis) were entered into the mixed models in the following incremental steps: (i) baseline value of the respective outcome, (ii) age, sex (male), daily use of antihypertension and/or heart medication (none), smoking status (never smoking and/or currently non-smoking), and either level of leisure-time physical activity (<2 hours/weeks light activity) or baseline cardiorespiratory fitness. The intervention effect estimates were reported as between-group mean difference, SE, 95% CI, and P-value.

A sensitivity analysis excluding participants reporting use of antihypertension and/or heart medication on a daily basis was performed using the same statistical methods. A secondary between-group analysis stratified on baseline level of aerobic workload (low <30% HRR or high ≥30% HRR) was conducted.

Results

Flow of participants

All of the three contacted companies agreed to participate. Researchers presented the study to 250 cleaners in the companies. Information meetings were arranged jointly with the company's obligatory employee meetings. In total, 137 (57%) wished to participate and were invited to the baseline measurement. Of those, 116 underwent baseline measurements and were randomized, with 57 assigned to the aerobic exercise group and 59 to the reference group. The main self-reported reasons for non-participation were lack of time (40%) or not finding the project relevant (11%).

After baseline measurements, 34 (29%) participants (19 from the aerobic exercise and 15 from the reference group) dropped out of the study and were lost to follow-up (figure 1). The main reasons given for dropping out were difficulties in making time for the project activities during working hours (24%) and being too tired to participate (18%); 27% did not give any reason.

Compliance

The 29% drop out was within the expected 30%. Participants randomized to the aerobic exercise participated on average in 51% of the planned sessions during the intervention period, including five participants with zero adherences. Participants not lost to follow-up, participated in 64% of the planned sessions, none with zero adherences. The reasons for missed sessions in the aerobic exercise group were vacation and days off (52%), medical appointments, hospitalization and/or sick leave (30%) or meetings at work, courses and/or urgent job tasks (18%). Overall, 94% of the planned sessions were offered as planned.

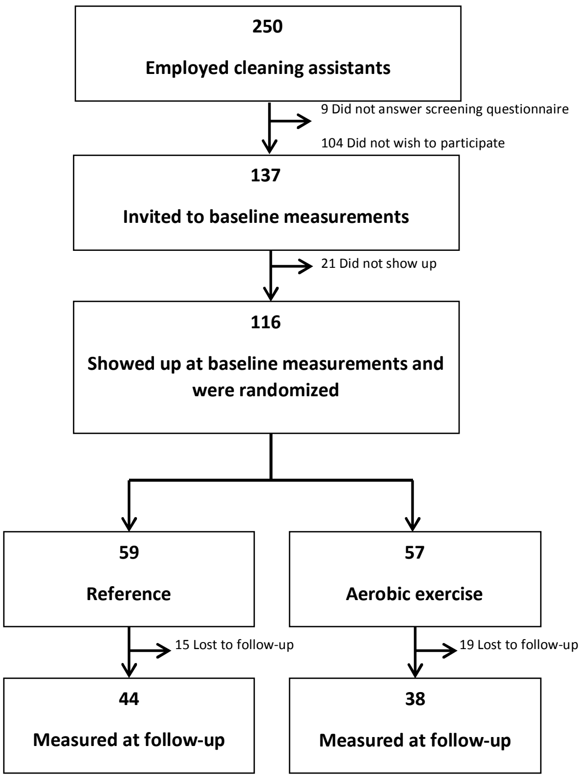

Figure 1. Flow chart of the participants in the study

After every fourth week of the intervention, the heart rate was monitored during the aerobic exercise session yielding an average HRR of 67 [standard deviation (SD) 13] %.

Baseline characteristics of the study population

The baseline characteristics of the study population are presented in table 1. Participants randomized to the intervention were mainly immigrants; 86% stated having a place of birth other than Denmark, 62% of whom were non-western.

No statistical or numerically significant differences between the randomized population and the population participating at both baseline and follow-up measurements (complete to follow-up) were found (data not shown), except for lower frequency of >12 years of education in the aerobic exercise group (5.3%) compared to the reference group (16.9%).

Compared to the randomized population (N=116), the 19 (33%) participants lost to follow-up in the exercise group were 2.5 years younger, included 1.7% fewer females, had a mean of 1 bpm higher SHR, 3.5% fewer used antihypertension and/or heart medication on a daily basis, 19.7% more were current smokers, and 5.2% more stated to have a leisure-time physical activity level ≥2 hours of moderate activity per week. Within the reference group, the 16 (25%) participants lost to follow-up were 0.9 years younger, included 3% fewer females, had a mean of 0.9 bpm higher SHR, a mean of 3.2 bpm higher RHR, 1 mmHg higher systolic BP, 3.5% less of them used antihypertension and/or heart medication on a daily basis, 14.6% more of them were current smokers, and 3.1% more of them stated to have a leisure time physical activity level of <2 hours of moderate activity per week.

The objective baseline HRR measures revealed that 51% of the randomized population exceeded recommended levels of relative aerobic workload during working hours (10, 11).

Intervention effects – within group

Fully adjusted within group changes of all outcomes during follow-up are shown in table 2. Cardiorespiratory fitness increased significantly by 7.2% or 1.8 (SE 0.7) ml $O_2 \times min^{-1} \times kg^{-1}$ (95% CI 0.3–3.2, P=0.02) in the aerobic exercise group and was reduced by 0.01% or -0.3 (SE 0.7) ml $O_2 \times min^{-1} \times kg^{-1}$ (95% CI -1.6–1.1, P=0.71) in the reference group.

Relative aerobic workload decreased in the aerobic exercise group and increased in the reference group. Both RHR and SHR decreased in the aerobic exercise group and increased in the reference group.

Systolic BP increased significantly by 5.2 (SE 1.2) mmHg (95% CI 2.8–7.6, P<0.01) in the aerobic exercise

Table 1. Description of the randomized study population at baseline (N=116), stratified by intervention group. Differences between aerobic exercise and reference groups were analyzed with student's t-test for continuous variables and with Chi² test for categorical variables. [SD=standard deviation; BP=blood pressure; HR=heart rate; HRR=heart rate reserve].

	Randomized group (N=116)				Aerobic exercise (N=57)				Reference (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 (females)			88	75.9			43	75.4			45	76.3
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		
Body mass index (kg/m²)	26.7	4.5			26.2	4.0			27.1	4.9		
Systolic BP (mmHg)	122.7	21.7			125.2	25.1			120.3	17.5		
Diastolic BP (mmHg)	82.7	12.6			83.7	14.2			81.7	10.8		
Body fat		8.6		31.6		8.3		31.1		8.9		32.1
Waist circumference (cm)	87.6	11.1			86.7	11.0			88.4	11.2		
Cardiorespiratory fitness (ml $O_2 \times min^{-1} \times kg^{-1}$)	24.9	6.6			24.8	5.8			25.0	7.2		
Resting HR (beats/minute)	71.3	14.8			71.7	10.6			70.5	8.8		
Sleeping HR (beats/minute)	49.5	5.8			49.2	6.5			49.7	5.1		
Aerobic workload (% HRR)		7.2		30.9		6.7		30.1		7.5		31.7
Steps taken per working hour (steps/hour)	1316	417			1271	343			1357	473		
Rating of perceived exertion during working hours	13.0	3.3			12.9	3.2			13.1	3.3		
Job seniority (years)	11.9	7.8			12.3	8.7			11.5	6.8		
Current smoker			28	24.1			13	22.8			15	25.4
Education (% >12 years of education)			13	11.2			3	5.3 [a]			10	16.9 [a]
Ethnicity (% non western)			72	62.1			40	70.2			32	54.2
Daily use of antihypertension and/or heart medication			14	12.1			8	14.0			6	10.2
Leisure-time physical activity (% <2 hours/weeks light activity or light activity 2–4 hours/weeks)			84	72.4			45	78.9			39	66.1
Physical activity at work (% having standing/walking work including lifts and strenuous physical work)			70	60.3			36	63.2			34	57.6

[a] Statistical significant difference between subgroups (P≤0.05).

group and less [1.3 (SE 1.1) mmHg, non-significant] in the reference group. Diastolic BP changes were <1 mmHg in both groups.

Intervention effects – between-groups

The between-group differences in 4-months change of primary and secondary outcomes are reported in table 3 for both model 1, adjusting for the baseline value of the respective outcome, and the fully-adjusted model 2. Effect sizes differed considerably (up to a factor of 4.4 or 444% in the case of aerobic workload) between models 1 and 2.

The fully adjusted (model 2) between-group difference in cardiorespiratory fitness change was 2.2 (SE 0.8) ml $O_2 \times min^{-1} \times kg^{-1}$ (95% CI 0.6–3.8, P<0.01) in the aerobic exercise group relative to the reference group. This corresponds to an 8.9% increase relative to the overall baseline mean in the randomized population.

Significant between-group differences were also found for changes in aerobic workload of -3.5 (SE 1.2) % HRR (95% CI -5.9– -1.0, P<0.01) (model 2). This corresponds to an 11.3% decrease relative to the overall baseline mean in the randomized population.

Significant between-group difference in change of RHR was -3.8 SE 1.2) bpm (95% CI -6.1– -1.4, P<0.01) (model 2). Relative to the overall baseline mean in the randomized population, this decrease corresponds to 5.3% (4 bpm). Similar results are seen for the change of SHR, the between-group difference was -3.8 (SE 1.1) bpm (95% CI -5.9– -1.7, P<0.01) (model 2). Relative to the overall baseline mean in the randomized population, this corresponds to a reduction of 7.7% (4 bpm).

The change in systolic BP showed significant between-group differences of 3.6 (SE 1.3) mmHg (95% CI 1.1–6.0, P<0.01) (model 2). Relative to the overall baseline mean in the randomized population, this change corresponds to a 2.9% (4 mmHg) increase. Diastolic BP changes did not differ significantly between groups.

Sensitivity analysis

A first sensitivity analyses excluded the 14 participants with daily use of antihypertension and/or heart medication and yielded between-group differences during follow-up comparable to results in the entire randomized population (N=116). For the 102 participants without such medication, the between-group changes from baseline to follow-up corresponded to a significant 6.0% increase in cardiorespiratory fitness for the aerobic exercise group, in the fully adjusted model (model 2).

In a second sensitivity analysis, model 2 for the aerobic workload was additionally adjusted for baseline and 4-month change in steps walked per hour of work (ie, indication of physical work demands), resulting in only a slightly (0.9%) higher estimate of change in relative

Table 2. Within group 4-month changes in cardiorespiratory fitness and secondary outcomes among cleaners (N=116) by intervention group. Results are based on a mixed-model analysis with step-wise entry of covariates in two models. [95% CI=95% confidence interval; SE=standard error; HR=heart rate; HRR=heart rate reserve; BP=blood pressure]

	Model 1 [a]				Model 2 [b]			
	ΔΔ	SE	95 % CI	P-value	Δ	SE	95 % CI	P-value
Aerobic exercise group (N=57)								
Primary outcome								
Cardiorespiratory fitness (ml $O_2 \times min^{-1} \times kg^{-1}$)	1.61	0.73	0.17–3.05	0.03	1.75	0.73	0.30–3.20	0.02
Secondary outcomes								
Aerobic workload (% of HRR)	-0.57	0.99	-2.52–1.39	0.57	-1.68	1.11	-3.90–0.54	0.14
Resting HR (beats/minute)	-1.72	1.06	-3.80–0.36	0.11	-1.37	1.14	-3.63–0.89	0.23
Sleeping HR (beats/minute)	-0.80	0.77	-2.32–0.73	0.30	-0.79	0.94	-2.66–1.08	0.40
Systolic BP (mmHg)	2.79	1.38	0.07–5.51	0.04	5.18	1.20	2.81–7.55	<0.01
Diastolic BP (mmHg)	-2.09	0.86	-3.79– -0.38	0.02	0.15	0.91	-1.64–1.94	0.87
Reference group (N=59)								
Primary outcome								
Cardiorespiratory fitness (ml $O_2 \times min^{-1} \times kg^{-1}$)	-0.24	0.68	-1.57–1.10	0.72	-0.25	0.68	-1.59–1.08	0.71
Secondary outcomes								
Aerobic workload (% of HRR)	0.03	0.90	-1.75–1.80	0.98	1.72	0.89	-0.05–3.49	0.06
Resting HR (beats/minute)	0.20	1.04	-1.84–2.25	0.85	2.28	1.06	0.20–4.37	0.03
Sleeping HR (beats/minute)	0.88	0.69	-0.48–2.24	0.20	2.90	0.77	1.37–4.43	<0.01
Systolic BP (mmHg)	0.91	1.34	-1.73–3.56	0.50	1.30	1.09	-0.86–3.46	0.24
Diastolic BP (mmHg)	-0.02	0.84	-1.86–1.45	0.81	-0.05	0.82	-1.68–1.58	0.95

[a] Model 1 is adjusted for baseline value of the respective outcome.

[b] For the primary outcome, Model 2 is additionally adjusted for age, sex, daily use of antihypertension and/or heart medication, smoking status and baseline leisure-time physical activity. For the secondary outcomes: Model 2 is additionally adjusted for age, sex, use of antihypertension and/or heart medication, smoking status and baseline cardiorespiratory fitness. The N differs between the different outcomes due to missing observations in covariate and/or outcome variables.

Table 3. Between-groups difference from baseline to 4-months follow-up on cardiorespiratory fitness and secondary outcomes in the randomized population of cleaners (N=116). Results are based on a mixed-model analysis with step-wise entry of covariates in two models. [95% CI=95% confidence interval; SE=standard error; HR=heart rate; HRR=heart rate reserve; BP=blood pressure]

	Model 1 [a]					Model 2 [b]				
	ΔΔ	SE	95 % CI	P-value	N	Δ	SE	95 % CI	P-value	N
Primary outcome										
Cardiorespiratory fitness (ml $O_2 \times min^{-1} \times kg^{-1}$)	1.81	0.78	0.27–3.36	0.02	86	2.21	0.79	0.64–3.78	<0.01	85
Secondary outcomes										
Aerobic workload (% of HRR)	-0.75	1.12	-2.96–1.47	0.50	85	-3.46	1.23	-5.92– -1.00	<0.01	61
Resting HR(beats/min)	-1.70	1.15	-3.97–0.56	0.14	115	-3.75	1.20	-6.13– -1.38	<0.01	85
Sleeping HR (beats/min)	-1.71	0.87	-3.43–<0.01	0.05	87	-3.82	1.05	-5.91– -1.73	<0.01	63
Systolic BP (mmHg)	2.28	1.49	-0.66–5.22	0.13	116	3.57	1.25	1.10–6.04	<0.01	86
Diastolic BP (mmHg)	-1.66	0.93	-3.50–0.17	0.08	116	-0.03	0.95	-1.90–1.84	0.98	86

[a] Model 1 is adjusted for baseline value of the respective outcome.

[b] For the primary outcome: Model 2 is additionally adjusted for age, sex, daily use of antihypertension and/or heart medication, smoking status and baseline leisure time physical activity. For the secondary outcomes: Model 2 is additionally adjusted for age, sex, use of antihypertension and/or heart medication, smoking status and baseline cardiorespiratory fitness. The N differs between the different outcomes due to missing observations in covariate and/or outcome variables.

aerobic workload [-3.6 SE 1.6), 95% CI -0.33– -6.87, P=0.03]. Moreover, no difference in number of steps taken per hour at work from baseline to follow-up was found in either of the groups.

A secondary between-group analysis stratified on baseline level of aerobic workload (low <30% HRR or high ≥30% HRR) and adjusted for the same covariates as in model 2. Those having a high level of aerobic workload at baseline (N=43) showed: 0.43 (SE 1.29) ml $O_2 \times min^{-1} \times kg^{-1}$ (95% CI -2.18–3.05, P=0.74) in cardiorespiratory fitness; -4.08 (SE 1.32) % HRR (95% CI -6.78– -1.39, P<0.01) for aerobic workload; -2.08 (SE 2.61) bpm (95% CI -7.37–3.20, P=0.43) for RHR; -8.01 (SE 1.73) bpm (95% CI -11.54– -4.49, P<0.01) for SHR; 6.65 (SE 2.46) mmHg (95% CI 1.68–11.63, P=0.01) for systolic BP; and 1.75 (SE 2.09) mmHg (95% CI -2.49–5.98, P=0.41) for diastolic BP. In the group of participants with a low level of aerobic workload at baseline (N=42), the results showed the following 3.95 (SE 1.47) ml $O_2 \times min^{-1} \times kg^{-1}$ (95% CI 0.98–6.92, P=0.01) in cardiorespiratory fitness; -2.99 (SE 1.89) % HRR (95% CI -6.82–0.85, P=0.12) for aerobic workload; -0.99 (SE 1.81) bpm (95% CI -4.65–2.66, P=0.59) for RHR; 0.09 (SE 1.25) bpm (95% CI -2.46–2.64, P=0.94) for SHR; 2.13 (SE 1.32) mmHg (95% CI -0.53–4.80, P=0.11) for systolic BP and -1.54 (SE 1.32) mmHg (95% CI -4.20–1.12, P=0.25) for diastolic BP.

Discussion

The main results of this study among cleaners were that the aerobic exercise group, in comparison with the reference group, significantly improved cardiorespiratory fitness, aerobic workload, SHR and RHR, but increased systolic BP.

Primary outcome

Between-group comparisons including all randomized participants show an average improved cardiorespiratory fitness in the aerobic exercise group of 2.2 (SE 0.8) ml $O_2 \times min^{-1} \times kg^{-1}$, corresponding to a 8.9% overall change compared to the randomized study population. In conclusion, the hypothesis regarding an enhanced cardiorespiratory fitness was not falsified. We consider this increase to be clinically relevant in this population because of their low baseline cardiorespiratory fitness [24.9 (SE 6.6) ml $O_2 \times min^{-1} \times kg^{-1}$] and because their aerobic workload already exceeded recommended levels. Previous worksite interventions have found similar effect sizes on cardiorespiratory fitness in both sedentary and physically demanding jobs (20, 21).

In order to achieve improvements in cardiorespiratory fitness, an exercise intensity of ≥60% of HRR is required (36). The average HRR during the aerobic exercise sessions in this study was 67 (SE 13)%, and 69% of the participants achieved an intensity of ≥60% of HRR. The observed low cardiorespiratory fitness of the cleaners [24.9 (SE 6.6) $O_2 \times min^{-1} \times kg^{-1}$] shows that the average relative aerobic workload during cleaning [31 (SE 7) % HRR) is at or above recommended levels (10, 11), but at the same time not designed (eg, in terms of sufficient intensity) to improve their cardiorespiratory fitness (24). There were 32 30-minute aerobic exercise sessions over the 4-month period. This indicates that as long as there are short periods of sufficiently high aerobic intensity, relatively few aerobic exercise sessions can increase cardiorespiratory fitness in this population. In summary, aerobic exercise with high intensity during paid working hours seems to improve cardiorespiratory fitness among cleaners.

Secondary outcomes

The aerobic exercise group significantly reduced the aerobic workload by 11.3% compared to the reference group. Therefore, the second hypothesis regarding a decreased aerobic workload was not falsified. To our knowledge, this is the first RCT finding positive effects on aerobic workload objectively measured during days of normal work. The aerobic workload measured at baseline was relatively high [31 (SE 7) % HRR). Such high aerobic workload is reported to cause strain on the cardiovascular systems (11), potentially leading to progression of arteriosclerosis (6, 22) and relates to an increased risk of cardiovascular disease (54). The observed reduction in aerobic workload of 11.3% HRR can therefore be considered of clinical relevance. HRR can be reduced by increases in cardiorespiratory fitness, leading to a reduced RHR and SHR, or a decreased physical work demand (14) or the combination of these two. The reduction of the aerobic workload in this study can therefore be explained by the increased cardiorespiratory fitness and the reduced SHR ($HRR = HR_{max} - SHR$) (48). Because changes in aerobic workload are also influenced by changes in the physical work demands, a sensitivity analysis additionally adjusting for change in steps walked per hour of work was applied. This additional adjustment for change in steps did not substantially change the between-group difference of aerobic workload displayed in table 3, model 2. In summary, this study supports the classic work physiology notion that an aerobic exercise intervention increasing cardiorespiratory fitness can reduce the relative aerobic workload among blue-collar workers (55).

The reductions of 5.3% in RHR and 7.7% in SHR reject the null hypothesis of no effects of the aerobic exercise intervention on RHR and SHR (56). Reductions in both RHR and SHR can potentially reduce the risk of both CVD and all-cause mortality (56–58).

Systolic BP increased by 5.2 (SE 1.2) mmHg in the aerobic exercise group compared to 1.3 (SE 1.1) mmHg in the reference group (table 2), leading to a between-groups change of 3.6 (SE 1.3) mmHg in fully adjusted analyses (table 3, model 2). Therefore, the null hypothesis of no effects is rejected for blood pressure. This finding is in accordance with the previously stated hypothesis of Krause and colleagues (22, 59) that high intensity physical exercise may cause an overload of the cardiovascular system when applied to workers with high levels of occupational physical activity, low cardiorespiratory fitness, and potentially limited ability for pauses and restitution.

An elevated systolic BP of 3.6 (SE 1.3) mmHg may appear relatively small, when applied to persons with low-to-normal BP (60). However, such an increase in BP is known to significantly increase CVD morbidity and mortality and, therefore, considered clinically relevant (61). Prediction of the long-term net cardiovascular health effects of this potentially harmful average BP change and the potential beneficial effects of an on average increased cardiorespiratory fitness is not possible with our data. It is conceivable that harmful and beneficial effects occur in different subsets of our population. Additional research is still needed to confirm if worksite aerobic exercise increases the systolic BP in other populations with high levels of occupational physical activity. Since ambulatory BP has been shown to be a better predictor of cardiovascular risk than resting BP (62), we plan additional analysis of our ambulatory BP data (35) and recommend that future studies with other populations should employ ambulatory BP measures.

To our knowledge, this study is the first to investigate the effects on BP of an aerobic exercise worksite intervention among cleaners. Our finding of an increased systolic BP is in contrast with previous exercise studies on BP among workers with high levels of occupational physical activity (20). The different effect in our study may be explained by the low cardiorespiratory fitness in our study population, making the participants less able to restitute from the additional aerobic exercise and, therefore, more susceptible to a cardiovascular overload. Of particular interest for interpretation of the study findings, the sub-group analyses stratified on aerobic workload at baseline showed that the participants exposed to a high aerobic workload (≥30% HRR during working hours) experienced a very strong increase in systolic BP of 6.5 (SE 2.5) mmHg (95% CI 1.7–11.6, P=0.01) from the aerobic exercise intervention, while the participants exposed to a low aerobic workload (<30% HRR during working hours) experienced a somewhat lower increase in systolic BP of 2.1 (SE 1.3 mmHg (95% CI -0.5–4.8, P=0.11). This finding supports the interpretation that the observed increased systolic BP in the intervention group could be explained by a cardiovascular overload from the aerobic exercise. However, because this analysis was not pre-planned, and the study was not designed to have sufficient power to investigate sub-group effects, these results should be interpreted with precaution.

The finding of an increased systolic BP in this single intervention is not enough evidence to draw general conclusions and recommendations. Therefore, it is important that this unintended adverse effect of this intervention will be monitored in additional future RCT among blue-collar workers. To reduce misclassification of BP, future measurements should be based on more frequent measures, ideally using 24-hour measures of ambulatory BP.

Strengths and limitations of the study

The cluster RCT design is a methodological strength reducing possible bias and contamination. Also the intention-to-treat analysis is a methodological strength reducing possible bias (63). Additionally, the external validity was enhanced by the creation of an aerobic exercise and reference group at each enrolled company. The study was sufficiently powered to detect clinically relevant changes. The frequency and intensity of the exercise training and all outcomes of the study were objectively measured, thereby decreasing the potential of self-reporting and selection bias. The mixed-model analysis is a strength when evaluating repeated measurements observations with observations missing at random, since the mixed-model analysis enables use of information from all observations without imputing missing observations (52). Regarding the intervention, the modified intervention mapping approach (35) is a strong feature since the intervention is tailored specifically to the individual needs and wishes of the participating company and its employees.

The convenience sampling of only three companies in the area of Copenhagen, Denmark, limits the generalizability of the findings.

Randomization was only partly successful, our multivariate analyses detected substantial amounts of residual confounding in effect measures in the process of adjusting for confounders. Without additional adjustment for age, sex, daily use of antihypertension and/or heart medication, smoking status, fitness, and baseline leisure-time physical activity in multivariate analyses, confounding by these factors would have obscured a large part of the intervention effects as can be seen by comparing effect sizes in model 2 against model 1, showing differences of up to 444%. Although there may still be residual confounding by other unknown factors, our multivariate analyses reduced potential confounding bias substantially.

Participants lost to follow-up had a lower cardiorespiratory fitness, higher mean aerobic workload and walked less during working hours at baseline compared to participants not lost to follow-up, causing a selection bias towards a more healthy population being followed up. In the aerobic exercise and reference groups, respectively, 19 and 15 were lost to follow-up (figure 1), this percentage (29%) of drop out is less than the expected 30% in our power calculations (39). No significant between-group differences were found among those lost to follow-up.

Missing data (missing not at random) occurred due to exclusions. At the cardiorespiratory fitness test, 18 (32%) participants were excluded at baseline and 10 (23%) at follow-up in the aerobic exercise group and 12 (20%) at baseline and 12 (27%) at follow-up in the reference group.

In the aerobic exercise group, 17 (30%) participants at baseline and 14 (37%) at follow-up, and 14 (24%) participants at baseline and 20 (45%) at follow-up in the reference group, did not have sufficiently high quality of data or were not mounted with the Actiheart.

Altogether, almost one fourth of the study population was excluded from testing possibly leading to a differential selection bias towards better outcomes in a more healthy population. On the other hand, the larger benefits in terms of enhanced cardiorespiratory fitness appeared among those with medication for pre-existing hypertension or heart disease. Due to some differences in missing data between groups, at baseline and follow-up, the mixed-model analysis was applied, since it allows an intention-to-treat analyses with missing observations (64).

Measurement of BP holds a large variability and is influenced by the context (eg, "white-coat hypertension"). However, large measurement variability typically increases random error and widens CI, ie, increases the risk for a type II error. Therefore, large measurement variability tends to bias results towards the null hypothesis and is not expected to cause a significant spurious effect in any one direction. Despite the small sample size in this RCT study, the measured BP effects were within 95% CI and thus do not indicate a high probability of such errors. Moreover, adjustment for several potential confounders makes it unlikely that the results were biased by confounding factors. For these reasons, it seems inappropriate to disregard the findings as systematically biased, and there is no indication of any differential misclassification bias that could possibly lead to a spurious increase in BP in the aerobic exercise group only.

Practical implications

Cleaners suffer from an increased risk of CVD (30, 31), partially due to their low cardiorespiratory fitness and high aerobic workload (24, 54). In fact, the extensive objective measurements revealed that more than half (51%) of our study population exceeded recommended levels of relative aerobic workload during working hours at baseline. Previous research has linked higher levels of aerobic workload with accelerated progression of atherosclerosis (22) and incidence of myocardial infarction (54). Clearly, there is a need to develop interventions that safely reduce aerobic workload and cardiovascular risk among high-risk occupational groups experiencing a high level of occupational physical activity (3).

The present study shows that the aerobic exercise worksite intervention improved cardiorespiratory fitness and most of the other measured cardiovascular risk factors with only 30 minutes of aerobic exercise twice a week for four months. The improvement in cardiorespiratory fitness, aerobic workload, RHR and SHR may reduce the risk of all-cause as well as CVD mortality (3, 26, 54, 56–58). On the other hand, the intervention significantly increased systolic BP, which may result in an increased risk of CVD and all-cause mortality (61, 65). Additional research is needed in order to provide effective and safe recommendations for how to promote cardiovascular health by aerobic exercise among workers with high relative aerobic workload and low cardiorespiratory fitness.

Concluding remarks

Based on a cluster-randomized design and objective data, this study indicates that a worksite aerobic exercise intervention among cleaners leads to improved cardiorespiratory fitness as well as reduced aerobic workload, RHR and SHR, but increases systolic BP. Accordingly, it seems like aerobic exercise induces several beneficial cardiovascular physiological effects but also one potentially harmful effect. Therefore, recommendations of aerobic exercise should take into consideration the potential cardiovascular overload of workers with high levels of occupational physical activity. Due to these contrasting findings, further studies are needed before recommendations with respect to aerobic exercise for workers with high levels of occupational physical activity can be made.

Conflict of interest

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Aerobic exercise reduces biomarkers related to cardiovascular risk among cleaners: effects of a worksite intervention RCT

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Abstract
Purpose Blue-collar workers have an increased risk of cardiovascular disease. Accordingly, elevated levels of biomarkers related to risk of cardiovascular disease, such as high-sensitive C-reactive protein, have been observed among blue-collar workers. The objective was to examine whether an aerobic exercise worksite intervention changes the level of inflammation biomarkers among cleaners.
Methods The design was a cluster-randomized controlled trial with 4-month worksite intervention. Before the 116 cleaners aged 18–65 years were randomized, they signed an informed consent form. The reference group ($n = 59$) received lectures, and the aerobic exercise group ($n = 57$) performed worksite aerobic exercise (30 min twice a week). Levels of biomarkers (high-sensitive C-reactive protein, fibrinogen, cholesterol, low- and high-density lipoprotein cholesterol and triglyceride) were collected at baseline and after 4 months. A repeated-measure, multi-adjusted, mixed-model intention-to-treat analysis was applied to compare between-group differences. The study was registered as ISRCTN86682076.
Results Significant ($p < 0.05$) between-group reductions from baseline to follow-up were found for high-sensitive C-reactive protein (−0.54 ± 0.20 μg/ml; 95 % CI −0.94, −0.14), low-density lipoprotein cholesterol (−0.32 ± 0.11 mmol/L; 95 % CI −0.54, −0.10) and the ratios of LDL/HDL (−0.30 ± 0.08; 95 % CI −0.46, −0.14), and LDL/TC cholesterol (−0.04 ± 0.02; 95 % CI −0.07, −0.01).
Conclusion This study indicates that an aerobic exercise intervention among cleaners leads to reduced levels of high-sensitive C-reactive protein and low-density lipoprotein cholesterol, and an unaltered level of fibrinogen. The aerobic exercise seems to improve inflammatory levels and lipoprotein profile among cleaners, with no signs of cardiovascular overload.

Keywords Worksite intervention · Aerobic workload · RCT · Blue-collar workers · Cardiovascular disease · Diurnal measurements · Objective measurements

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Introduction

Blue-collar workers have an increased risk of cardiovascular disease (Li et al. 2013; Zöller et al. 2012). Accordingly, elevated levels of inflammation biomarkers, such as high-sensitive C-reactive protein (hsCRP), have been observed among blue-collar workers (Kittel et al. 2002; Clark et al. 2012). In addition, blue-collar workers are reported to have an unfavourable lipoprotein profile, with increased levels of triglyceride (TG) and total cholesterol (TC), and a high ratio of low-density lipoprotein (LDL cholesterol)/high-density lipoprotein (HDL cholesterol) (Clark et al. 2012;

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Khanolkar et al. 2012). Interventions targeting the elevated inflammatory levels and unfavourable lipoprotein profile to prevent cardiovascular disease among blue-collar workers are therefore requested.

Many factors, like diet, smoking and physical activity, influence levels of inflammatory biomarkers and the lipoprotein profile both separately and in combinations, as described in previous literature (Grandjean et al. 1996; Pedersen and Saltin 2006). Also, aerobic exercise has been previously shown to effectively reduce levels of inflammation biomarkers (Okita et al. 2004; Loprinzi et al. 2013; Plaisance and Grandjean 2006; Kasapis and Thompson 2005) and thereby risk of cardiovascular disease (Danesh et al. 2005; Kaptoge et al. 2010; de Ferranti and Rifai 2007). This may be explained by the adaptations from aerobic exercise leading to a lowered acceleration of the inflammation in the arterial endothelia initiated by a lowered LDL concentration. Since the hsCRP binds to the LDL, it is thereby also lowered (de Ferranti and Rifai 2007; Kasapis and Thompson 2005; Lusis 2000). Aerobic exercise is therefore recommended to prevent the excessive risk of cardiovascular disease among blue-collar workers (Li et al. 2013; Zöller et al. 2012). However, we are not aware of previous studies that have evaluated the effect of an aerobic exercise worksite intervention on inflammatory biomarkers in a blue-collar population. The worksite is a recommended arena for physical activity interventions (Heath et al. 2012), mainly because it offers opportunities to reach specific high-risk groups exposed to similar risk factors.

Blue-collar workers, such as cleaners, are often exposed to high volumes of occupational physical activity (Steele and Mummery 2003; Søgaard et al. 2006). Although the volume of occupational physical activity is relatively high (Bonjer 1971), the intensity is not sufficiently high to enhance the cardiorespiratory fitness (Korshøj et al. 2013; Ruzic et al. 2003). Therefore, it may be hypothesized that aerobic exercise could enhance the cardiorespiratory fitness among workers with high levels of occupational physical activity. Thus, the initial combination of a high volume of occupational physical activity, limited possibility for recovery and a low level of cardiorespiratory fitness could overload the cardiovascular system (Clays et al. 2014; Holtermann et al. 2012; Krause et al. 2007). An aerobic exercise intervention, increasing the volume and intensity of physical activity, may therefore progress a potential overload of the cardiovascular system (Krause et al. 2007; Armstrong et al. 2015; Schnohr et al. 2015; Lee et al. 2014) and thereby lead to increased levels of inflammation and risk of cardiovascular disease (Danesh et al. 2005; Kaptoge et al. 2010; de Ferranti and Rifai 2007).

Recently, we found a general reduction in risk factors for cardiovascular disease, but also a clinically significant increased systolic blood pressure following a worksite aerobic exercise randomized controlled intervention among cleaners (Korshøj et al. 2015). This finding indicates that aerobic exercise may overload the cardiovascular system of cleaners, possibly due to their high exposure to occupational physical activity (Søgaard et al. 2006; Krüger et al. 1997), limited possibility for recovery and low level of cardiorespiratory fitness (Korshøj et al. 2013; Louhevaara 1999; Ruzic et al. 2003). Thus, the effects on inflammatory levels and lipoprotein profile of aerobic exercise interventions among cleaners are of particular interest for investigation.

The objective was therefore to examine the effects of an aerobic exercise intervention on inflammatory levels and lipoprotein profile among cleaners. The null hypothesis of the study was that the aerobic exercise intervention would not modify the inflammatory levels and lipoprotein profile.

Methods

Study design

The study design represents a cluster-randomized controlled trial. The intervention was divided into two phases with different aims. The aim of the first intervention phase, from baseline to 4-month follow-up, was to evaluate the efficacy of the intervention on biomarkers related to cardiovascular risk (Korshøj et al. 2012).

The study was approved by the Danish Data Protection Agency and the Ethics Committee for the regional capital in Denmark (journal number H-2-2011-116) and subsequently conducted in accordance with the Declaration of Helsinki. The study was registered as ISRCTN86682076 in Current Controlled Trials (Current Controlled Trials 2014).

Recruitment

Recruitment is described in detail in the protocol paper (Korshøj et al. 2012). Briefly described, the recruitment took place by directly contact to the management of cleaning companies. By confirmation of collaboration, all employees were invited to an information meeting. At the information meeting, the cleaners filled in a screening questionnaire that collected background information such as ethnicity, smoking status and job seniority. Additionally, the cleaners were asked whether they wished to participate in the study. All participants signed an informed consent form agreed upon by the Ethics Committee for the regional capital in Denmark. The authors confirm that all ongoing and related trials for this intervention are registered.

Study population

The study population comprised cleaners performing predominantly cleaning in day-care institutions, offices, hospitals and schools. At company level, the inclusion criteria were more than 50 employed cleaners and the possibility of the cleaners participating in the project activities during paid working hours. Eligibility criteria were: employment as a cleaner for >20 h per week; age 18–65 years; and the provision of signed and informed consent. Exclusion criteria were pregnancy and fever on the day of testing. Further exclusion criteria for specific physical tests and blood sampling were moderate and severe hypertension (≥160/≥100 mmHg), angina pectoris, cardiac insufficiency and acute myocardial infarction. The sample size was based on a power calculation on the proposed intervention effect (increase by 4 %) on cardiorespiratory fitness (mlO_2/min/kg) and showed that it would take 52 participants in each of the two intervention groups to show significance at a level of 0.05. The sample size calculations assumed recruitment of 40 % of eligible cleaners and a dropout rate of 30 % during the intervention (Korshøj et al. 2012).

Randomization

A full description of the randomization is reported elsewhere (Korshøj et al. 2012). The randomization was performed at cluster level, and clusters were set within strata. Each stratum was formed according to the manager to whom the participant reports, and the clusters were balanced in respect of geographical work location, gender, age and job seniority. Participants were randomly assigned to either a reference group or an aerobic exercise group.

Intervention

Participants assigned to the aerobic exercise group received 30 min of supervised aerobic exercise training twice a week for 16 weeks at an intensity ≥60 % of maximal oxygen consumption. The type of aerobic exercise was tailored to the specific workplace (Korshøj et al. 2012) via an intervention mapping approach (Bartholomew et al. 1998).

The reference group received two lectures of 2-h duration during the 4-month period. The lectures concerned healthy living, and the participants were invited to give suggestions for the lectures. None of the lectures addressed physical activity.

Data collection

The baseline measurements were conducted in January 2012 at the first company, May 2012 at the second company and August 2012 at the third company. Follow-up measurements were conducted in May/June 2012 at the first company, January/February 2013 at the second company and February 2013 at the third company, corresponding to follow-up periods of approximately 16 weeks at the first company, 27 weeks (including 10 weeks of summer holidays) at the second company and 18 weeks (including 2 weeks of Christmas holidays) at the third company. The data collection consisted of a questionnaire-based interview including items regarding sociodemographics, lifestyle, ethnicity, education level, job seniority, gender, diagnosed illnesses, use of medication, level of physical activity at work and in leisure time (Saltin and Grimby 1968), and rating of perceived exertion during working hours (Borg 1962). Additionally, measurements of anthropometrics, blood pressure, and blood sampling and fixing of the monitors for the diurnal objective measurements of heart rate were conducted.

Physiological measurements

Height was measured without shoes in an upright standing position (Seca 213, Birmingham, UK). Body weight, body mass index (BMI) and body fat percentage were determined using bioelectrical impedance analysis (TANITA BC-418, USA). Resting blood pressure was measured three times on the left arm after at least 15 min sitting at rest in a quiet room (Omron M6 comfort, Omron, Helsinki, Finland) (O'Brien et al. 2005). The waist was defined as the narrowest point between the lowest rib and the iliac crest (Canoy 2008). Level of cardiorespiratory fitness was estimated by a sub-maximal step test (Aadahl et al. 2013) conducted on a bench of 30 cm height for females and 35 cm for males.

Diurnal measurements of heart rate

The participants were asked to wear the monitor 24 h a day. The Actiheart heart rate monitor (CamNtech, Cambridge, UK) was worn for 4 days (two working and two non-working days) and was able to measure continuously as it is water resistant and wireless. The participants were asked to keep an activity log of working hours and sleeping time. Actiheart was initialized and data downloaded using the commercial software (version 4.0.98, CamNtech, Cambridge, UK). Actiheart measures electrocardiographic raw signals by inter-beat intervals with a sensitivity of 0.25 mV (The Actiheart web site 2014). Actiheart is validated for measurement of heart rate, heart rate variability and estimations of energy expenditure in the field (Barreira et al. 2009; Assah et al. 2011). The Actiheart monitors were attached to the skin using two ECG electrodes (Ambu blue sensor VL-00-S/25, Ballerup, Copenhagen;

Denmark) at either of the two validated positions at the apex of the sternum, orthogonally to the wire axis, with a horizontal wire to the left, or at the manubrium of the sternum, orthogonally to the wire axis, with a horizontal wire to the left (Brage et al. 2005).

Blood sampling

Non-fasting blood samples were taken during working hours (7 a.m. to 3 p.m.), and no restrictions were imposed with regard to food, caffeine, tobacco and alcohol consumption or exercise prior to the sampling. The blood samples were stored at −20 °C and ethylenediaminetetraacetic acid plasma at −80 °C until analysed within a maximum of 2 years.

High-performance liquid chromatography (HPLC) with a cation exchange column, Mono S HR 5/5 from Pharmacia Biotech AB, Uppsala, Sweden, was used to determine HbA_{1c}. The HPLC consisted of a Waters 625 LC system together with a Waters photodiode array detector model 996 and a WISP 717 auto-sampler for automatic injection of the samples. Millennium chromatography software was used to calculate concentrations (Waters Associates Inc., Milford, US). The method for HbA_{1c} has been evaluated by inter-laboratory comparison based on 17 patient samples and found to be linear in the range 4.1–14.3 % of total haemoglobin and without systematic bias (Garde et al. 2000). Lyphochek Diabetes Control (Calibrator) from Bio-Rad (Anaheim, CA, US) for HbA_{1c} was used to monitor the long-term stability of the method.

HDL cholesterol, LDL cholesterol and TC were analysed using a Cobas MIRA Plus. The determination of HDL cholesterol, LDL cholesterol, TC and TG was carried out by ABX Pentra assays from Triolab (Sollentuna, Sweden). Calculation of LDL/HDL cholesterol ratio and LDL/TC cholesterol ratio was carried out by dividing LDL cholesterol by HDL cholesterol and LDL cholesterol by TC. The analytical methods for measuring TC in serum have been validated (Christensen et al. 1993; Hansen et al. 2007). Commercially available control samples for HDL cholesterol, LDL cholesterol, TC and TG were analysed together with the samples to show equivalence between different runs. Westgard control charts were used to document that the analytical methods remained in analytical and statistical control, i.e. the precision and trueness of the analytical methods remained stable (Westgard et al. 1981).

Fibrinogen was analysed by turbidimetry on Cobas MIRA Plus. We used a high-sensitive ELISA (EU59151), purchased from IBL, International GMBH, Hamburg, Germany, to measure hsCRP. The between-assay variation was 5.8 % at 1.6 µg/ml, and the limit of detection was 0.02 µg/ml.

Analyses

The primary outcome in this paper is between-group changes in hsCRP, fibrinogen, HDL cholesterol, LDL cholesterol, TC, TG and HbA_{1c} during the 4 months of follow-up. From the diurnal measures, only heart rate measurements with beat error ≤50 % were included (Skotte et al. 2014) in order to only include diurnal measurements of sufficient quality in the statistical analysis. The relative aerobic workload was calculated as HRR ($HRR = HR_{max} - SHR$) (Karvonen and Vuorimaa 1988), the difference between the estimated maximal heart rate (HR_{max}) (Tanaka et al. 2001) and the sleeping heart rate (SHR), defined as the 10th lowest recorded heart rate value during sleep (Brage et al. 2004). The percentage of the HRR was calculated as [$\%HRR = ((\text{HR during activity} - SHR)/HRR) \times 100$].

Statistical analyses

The analyses were performed according to the intention-to-treat (ITT) principle, in which all randomized participants are included in the statistical analyses. Missing values were not imputed either for outcome or for covariate variables (White et al. 2012; Twisk et al. 2013). The analyses were performed to evaluate the between- (aerobic exercise compared to reference) and within-group effects on the outcomes of the 4-month intervention period (follow-up baseline). Analyses followed a repeated-measures 2 × 2 mixed-model design. Independent categorical variables (fixed factors) were group (aerobic exercise and reference), measurement time (baseline and 4-month follow-up) and the interaction between groups and measurement time. Participants were entered in the model as a random effect nested in clusters (i.e. to account for the cluster-based randomization). Covariates to be included were chosen based on baseline differences between groups on theoretically considered confounders and their statistical association with the group and measurement time. The following covariates were incrementally taken into account in the analysis (reference value in parenthesis): baseline value of the respective outcome, age, gender (male), BMI, daily use of cholesterol and/or hormone medication (none), smoking status (never smoked and/or currently non-smoking), level of leisure-time physical activity (<2 h per week of light activity) and alcohol consumption. The covariates were included in the mixed model in two models: the model step included adjustment for the baseline value of the respective outcome, while the second model included additional adjustment for age, gender, BMI, use of cholesterol and/or hormone medication, smoking status, alcohol consumption and leisure-time physical activity. The statistical estimates of the outcomes are reported as between-group mean difference ± SE, 95 % confidence interval and level of

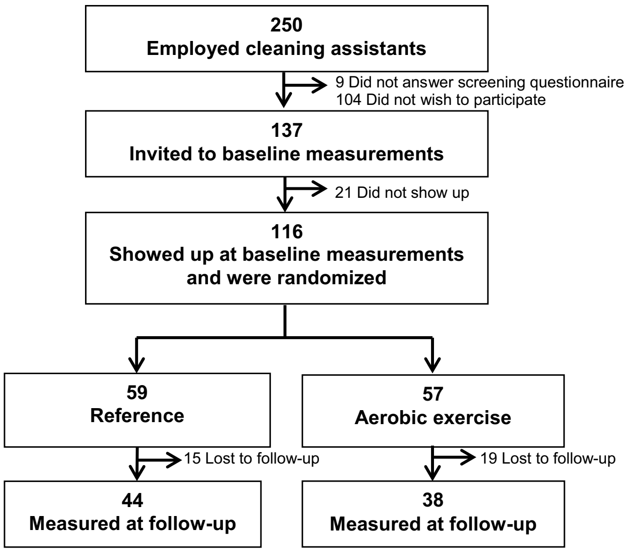

Fig. 1 Flow chart for the participants

significance, where a level of ≤0.05 was set as the level of statistical significance.

Sensitivity analysis was performed by applying the same statistical model with the exclusion of participants reporting daily use of cholesterol and/or hormone medication. Additionally adjustment for western/non-western ethnicity was applied to the fully adjusted model 2 in the between-group analysis.

All statistical analyses were conducted using IBM SPSS statistical software (version 21) (Armonk, NY, US) and the SAS statistical software for Windows (version 9.3) (Cary, NC, US).

Results

Flow of participants

Of the three companies contacted, all agreed to participate. At these companies, 250 cleaning assistants were introduced to the project. Of those, 137 (45 %) wished to participate and were invited to the baseline measurements. At the baseline measurements, 116 participated and were randomized, with 59 assigned to the reference group and 57 to the aerobic exercise group. Of those participants who were randomized, 34 (29 %) dropped out of the project and were lost to follow-up (15 from the reference group and 19 from the aerobic exercise group) (Fig. 1), (Korshøj et al. 2015).

Compliance

The real dropout in this study (29 %) was below the expected dropout (30 %) from baseline to follow-up. On average, the participants randomized to the aerobic exercise took part in 51 % of the planned sessions during the intervention period, including a total of five participants with zero adherences. Those participants not lost to follow-up participated in 64 % of the planned sessions, with no zero adherences (Korshøj et al. 2015).

After every fourth week of intervention, heart rate was monitored at three time-points during the aerobic exercise session, yielding an average heart rate of 67 (±13 SD) % HRR (Korshøj et al. 2015).

Baseline characteristics of the study population

Table 1 presents the baseline characteristics of the study population. The only significant difference between the aerobic exercise group and the reference group was the length of education, where a higher amount of participants in the reference group had >12 years of education. Additionally, no statistical or numerically significant differences were observed between the randomized population and the population participating either at baseline or at the follow-up measurements (complete to follow-up). Within the aerobic exercise group, the 19 participants (33.3 %) lost to follow-up had different numerical values to the true population on the following parameters: age (2.5 years younger), gender (1.7 % less females), smoking (19.7 % more smokers) and leisure-time physical activity (5.2 % more stated to be active ≥2 h of moderate activity per week). Within the reference group, the 16 participants (25.4 %) lost to follow-up had different numerical values to the true population on the following parameters: age (0.9 years younger), gender (3,0 % less females), smoking (14.6 % more smokers) and leisure-time physical activity (3.1 % more stated to be active ≥2 h of moderate activity per week) (Korshøj et al. 2015).

Between-group intervention effects

Table 2 presents the between-group differences in the intervention-induced change in biomarkers from baseline to follow-up. The aerobic exercise group significantly decreased the level of hsCRP in comparison with the reference group by 33 % (model 1) relative to the overall baseline mean in the randomized population. The fully adjusted model (model 2) showed a between-group difference in hsCRP change corresponding to 37 % in the aerobic exercise group. Non-significant between-group changes in fibrinogen were found in both model 1 and the fully adjusted model (model 2).

No between-group difference was found in the change in HDL cholesterol in either model 1 or the fully adjusted model (model 2). Both model 1 and the fully adjusted model (model 2) showed a significant between-group difference in LDL cholesterol change. In model 1, this difference corresponded to a decreased level of LDL cholesterol

Table 1 Description of randomized study population at baseline measurements ($N = 116$), stratified in the aerobic exercise group ($n = 57$) and reference group ($n = 59$). Mean ± SD is reported

	Randomized population ($N = 116$)			Aerobic exercise ($n = 57$)			Reference ($n = 59$)		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*
Age (years)	45.3	8.6		44.9	9.2		45.7	8.1	
Gender (% of females)	75.9		88	75.4		43	76.3		45
Height (m)	1.63	0.09		1.63	0.09		1.62	0.08	
Weight (kg)	70.7	14.1		69.7	12.7		71.7	15.4	
Body mass index (kg/m^2)	26.7	4.5		26.2	4.0		27.1	4.9	
Systolic blood pressure (mmHg)	122.7	21.7		125.2	25.1		120.3	17.5	
Diastolic blood pressure (mmHg)	82.7	12.6		83.7	14.2		81.7	10.8	
Waist circumference (cm)	87.6	11.1		86.7	11.0		88.4	11.2	
Cardiorespiratory fitness (mlO$_2$/min/kg)	24.9	6.6		24.8	5.8		25.0	7.2	
Resting heart rate (beats/min)	71.3	14.8		71.7	10.6		70.5	8.8	
Sleeping heart rate (beats/min)	49.5	5.8		49.2	6.5		49.7	5.1	
Aerobic workload (% of HRR)	30.9	7.2		30.1	6.7		31.7	7.5	
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 >12 years education)	11.2		13	5.3*		3	16.9*		10
Ethnicity (% non-western)	62.1		72	70.2		40	54.2		32
Daily use of cholesterol and/or hormone medication (%)	13.8		16	12.3		7	15.3		9
Leisure-time physical activity (% <2 h/week light activity or light activity 2–4 h/week)	72.4		84	78.9		45	66.1		39
Physical activity at work (% having standing/walking work including lifts and strenuous physical work)	60.3		70	63.2		36	57.6		34
High-sensitive C-reactive protein (μg/mL)	1.47	1.72		1.39	1.30		1.53	2.05	
Fibrinogen (g/L)	3.22	0.68		3.24	0.69		3.19	0.67	
High-density lipoprotein (mmol/L)	1.53	0.39		1.53	0.36		1.53	0.41	
Low-density lipoprotein (mmol/L)	3.32	1.00		3.50	0.98		3.16	1.00	
Total cholesterol (mmol/L)	5.66	1.25		5.82	1.25		5.50	1.24	
Triglyceride (mmol/L)	1.45	0.77		1.48	0.82		1.42	0.71	
Glycated haemoglobin (%)	5.24	0.65		5.29	0.77		5.20	0.51	
Low-density lipoprotein/high-density lipoprotein ratio	2.28	0.82		2.38	0.76		2.19	0.87	
Low-density lipoprotein/total cholesterol ratio	0.58	0.08		0.60	0.08		0.57	0.08	

Differences between aerobic exercise and reference groups in continuous variables are analysed using a Student's *t* test, and categorical variables are analysed using a Chi-square test

* Significant between-group difference ($p \leq 0.05$)

for the aerobic exercise group corresponding to 9 % relative to the reference group. In the fully adjusted model (model 2), this difference corresponded to 10 %. Non-significant between-group changes in TC were found in both of the models (models 1 and 2). A significant between-group difference in TG change was seen in model 1. This difference corresponded to an increased level of TG for the aerobic exercise group corresponding to 16 % relative to the reference group. When analysing the level of TG in the fully adjusted model (model 2), no statistical between-group changes were seen. Non-significant between-group changes in HbA_{1c} were found in both of the models (models 1 and 2). Due to missing covariate observations, the fully adjusted model (model 2) did not converge, except when the adjustment for alcohol was not taken into account. When evaluating the between-group difference in the change in LDL/HDL cholesterol ratio, a significant decrease was observed corresponding to 12 % in the aerobic exercise group relative to the reference group (model 1). The fully adjusted model (model 2) revealed a similar difference corresponding to a 13 % decrease for the aerobic exercise group. Both model 1 and the fully adjusted model (model 2) show a significant between-group difference in the change in LDL/TC cholesterol

Table 2 Between-group difference (mean ± SE) from baseline to 4-month follow-up on the outcomes in the randomized population of cleaners ($N = 116$)

	Model 1					Model 2				
	Δ	SE	95 % CI	*p*	*n*	Δ	SE	95 % CI	*p*	*n*
Δ High-sensitive C-reactive protein (μg/mL)	−0.48	0.20	−0.87, −0.09	0.02	102	−0.54	0.20	−0.94, −0.14	<0.01	93
Δ Fibrinogen (g/L)	−0.13	0.09	−0.31, 0.05	0.15	102	−0.13	0.10	−0.33, 0.06	0.18	93
Δ High-density lipoprotein (mmol/L)	<−0.01	0.03	−0.05, 0.05	1.00	102	0.01	0.03	−0.04, 0.06	0.72	93
Δ Low-density lipoprotein (mmol/L)	−0.30	0.11	−0.51, −0.09	<0.01	102	−0.32	0.11	−0.54, −0.10	<0.01	93
Δ Total cholesterol (mmol/L)	−0.21	0.12	−0.44, 0.02	0.08	102	−0.24	0.13	−0.50, 0.01	0.06	93
Δ Triglyceride (mmol/L)	0.23	0.11	0.02, 0.44	0.03	102	0.18	0.10	−0.02, 0.39	0.08	93
Δ Glycated haemoglobin (%)[a]	0.01	0.05	−0.09, 0.10	0.92	102	0.04	0.05	0.06, −0.14	0.40	93
Δ Low-density lipoprotein/high-density lipoprotein ratio	−0.27	0.08	−0.42, −0.12	<0.01	102	−0.30	0.08	−0.46, −0.14	<0.01	93
Δ Low-density lipoprotein/total cholesterol ratio	−0.04	0.02	−0.07, −0.01	0.02	102	−0.04	0.02	−0.07, −0.01	0.03	93

Between-group 95 % confidence interval and level of significance are reported

Results are based on a mixed-model analysis with step-wise entry of covariates in two models

Model 1 is adjusted for the baseline value of the respective outcome

Model 2 is additionally adjusted for age, gender, BMI, daily use of cholesterol and/or hormone medication, smoking, alcohol consumption and leisure-time physical activity

n differs between model 1 and model 2 due to missing observations in covariate and/or outcome variables

[a] Due to missing data in the covariates, model 2 did not converge for HbA_{1c}, so the estimates for this outcome are not adjusted for alcohol in model 2

Table 3 Within-group difference (mean ± SE) from baseline to 4-month follow-up on the outcomes in the randomized population of cleaners ($N = 116$)

	Aerobic exercise group				Reference group			
	Δ	SE	95 % CI	*p*	Δ	SE	95 % CI	*p*
Δ High-sensitive C-reactive protein (μg/mL)	−0.41	0.19	−0.04, −0.78	0.03	0.17	0.18	−0.18, 0.53	0.34
Δ Fibrinogen (g/L)	0.14	0.09	−0.04, 0.33	0.12	0.28	0.09	0.10, 0.45	<0.01
Δ High-density lipoprotein (mmol/L)	−0.03	0.02	−0.08, 0.02	0.23	−0.04	0.02	−0.09, 0.00	0.07
Δ Low-density lipoprotein (mmol/L)	−0.88	0.10	−1.09, −0.68	<0.01	−0.56	0.10	−0.36, −0.75	<0.01
Δ Total cholesterol (mmol/L)	−0.31	0.12	−0.54, −0.07	0.01	−0.03	0.11	−0.25, 0.19	0.78
Δ Triglyceride (mmol/L)	0.37	0.10	0.18, 0.56	<0.01	0.20	0.09	0.02, 0.38	0.03
Δ Glycated haemoglobin (%)[a]	0.11	0.05	0.02, 0.20	0.02	0.07	0.05	−0.02, 0.16	0.11
Δ Low-density lipoprotein/High-density lipoprotein ratio	−0.59	0.08	−0.74, −0.44	<0.01	−0.30	0.07	−0.44, −0.15	<0.01
Δ Low-density lipoprotein/Total cholesterol ratio	−0.13	0.02	−0.17, −0.10	<0.01	−0.09	0.02	−0.06, −0.12	<0.01

Within-group 95 % confidence interval and level of significance are reported

Results are based on a mixed-model analysis with step-wise entry of covariates in two models. Only the fully adjusted model is presented here

Model 2 is adjusted for baseline value of the respective outcome, age, sex, BMI, daily use of cholesterol and or hormone medication, smoking, alcohol and leisure-time physical activity

[a] Due to missing data in the covariates, model 2 did not converge for HbA_{1c}, so the estimates for this outcome are not adjusted for alcohol in model 2

ratio corresponding to a decrease of 7 % for the aerobic exercise group in relation to the reference group.

Within-group intervention effects

The fully adjusted within-group differences (model 2) from baseline to follow-up are presented in Table 3. The aerobic exercise group significantly decreased the level of hsCRP by 29 %, LDL by 25 %, TC by 5 %, the LDL/TC ratio by 22 % and LDL/HDL ratio by 25 %. Additionally, significant increases were seen for the levels of TG by 25 % and HbA_{1c} by 2 %.

Within the reference group, the fully adjusted within-group differences (model 2) from baseline to follow-up showed significantly decreased levels of LDL by 37 %, LDL/HDL ratio by 14 % and LDL/TC ratio by 16 %. Additionally, significant increases were seen for the levels of fibrinogen by 9 % and TG by 14 %.

Sensitivity analysis

After excluding participants reporting a daily use of cholesterol and/or hormone medication ($n = 16$), the analysis yields similar between-group differences from baseline to follow-up in the fully adjusted model (model 2), except for the LDL/TC ratio, where the sensitivity analysis did not reach statistical significance. In this population without daily use of cholesterol and/or hormone medication ($n = 100$), the within-group changes from baseline to follow-up are similar to the results in the randomized population.

By further adjusting for baseline occupational physical activity, similar between-group results are obtained. Also, when additionally adjusting for ethnicity (western/non-western), similar between-group results are obtained.

Discussion

Summary of results

The main results of this study are that the aerobic exercise group, compared with the reference group, significantly decreased levels of hsCRP, LDL cholesterol, and LDL/HDL and LDL/TC cholesterol ratios after the 4-month intervention period. No between-group differences were observed for fibrinogen, HDL cholesterol and HbA_{1c}. Thus, aerobic exercise seems to improve inflammatory levels and lipoprotein profile among cleaners, with no signs of cardiovascular overload.

Change in biomarkers

Between-group comparisons including all randomized participants show a 37 % decrease in hsCRP in the aerobic exercise group. A difference of this magnitude can be considered clinically relevant, as this lowered level would be expected to decrease the risk of cardiovascular death (Kaptoge et al. 2010). Based on this reduced level of hsCRP, the null hypothesis considering hsCRP can be falsified. No between-group differences in the level of fibrinogen following the intervention were found.

Previous studies indicate that moderate-to-high-intensity aerobic exercise decreases the levels of inflammatory biomarkers such as hsCRP and fibrinogen (Okita et al. 2004; Loprinzi et al. 2013; Plaisance and Grandjean 2006; Kasapis and Thompson 2005) when applied along with sufficient recovery (Knez et al. 2006). The introduction of the aerobic exercise intervention was therefore expected to reduce the levels of inflammatory biomarkers (Okita et al. 2004; Loprinzi et al. 2013; Plaisance and Grandjean 2006; Kasapis and Thompson 2005), as shown for hsCRP. These studies (Okita et al. 2004; Loprinzi et al. 2013; Plaisance and Grandjean 2006; Kasapis and Thompson 2005) were conducted as studies of healthy populations and not of blue-collar workers in particular. This study finds similar effects of aerobic exercise to the previous studies on hsCRP, but not fibrinogen, and not indicating any cardiovascular overload.

The between-group differences following the intervention showed a significantly reduced level of LDL cholesterol for the aerobic exercise group of 10 %. This reduction is considered clinically significant, as it corresponds to a decreased risk of cardiovascular events (Delahoy et al. 2009). People exposed to an energy expenditure above 2200 kcal/week do not seem to benefit from additional physical activity energy expenditure with respect to levels of lipoprotein (Durstine et al. 2001; Hurley et al. 1988). Cleaners are generally exposed to an energy expenditure above 2200 kcal/week (Krüger et al. 1997), and consequently, the reduced level of LDL cholesterol was not expected. Our study therefore indicates that additional moderate-to-high-intensity aerobic exercise may benefit the level of LDL cholesterol among cleaners, in spite of their baseline level of energy expenditure. Accordingly, the null hypothesis regarding no change in levels of lipoproteins between groups is falsified for LDL cholesterol and for LDL/HDL and LDL/TC cholesterol ratios. The initial energy expenditure may be one explanation of why the other measured lipoproteins did not show significant between-group differences following the intervention in the fully adjusted model (model 2, Table 2).

As for lipoproteins, the level of HbA_{1c} is affected by the general level of energy expenditure and not the intensity of physical activity (Umpierre et al. 2011). Accordingly, the analysis did not show significant between-group differences in the level of HbA_{1c} following the intervention (model 2, Table 2).

Practical implications

Improved knowledge of how to reduce cardiovascular risk among blue-collar workers is needed (Li et al. 2013). Cleaners have increased risk of cardiovascular disease (Zöller et al. 2012; Sjögren et al. 2003) and therefore constitute a relevant study population for preventive interventions, such as this study. This study showed that just 30 min of worksite aerobic exercise at a moderate-to-high intensity ($\geq$60 % of relative heart rate) twice a week for 4 months during paid working hours (Korshøj et al. 2012) reduced levels of hsCRP and LDL cholesterol, and LDL/HDL and

LDL/TC cholesterol ratios. Based on the biomarkers of inflammation, this study shows no signs of the possible cardiovascular overload among workers with high occupational physical activity. Because of the overall reduction in risk factors for cardiovascular disease, but also an increased systolic blood pressure (Korshøj et al. 2015), the effects of aerobic exercise among cleaners seem beneficial, but special attention to blood pressure is encouraged.

Methodological considerations—strengths and limitations

The cluster-randomized controlled trial design and the ITT analysis (Detry and Lewis 2014) represent strengths, reducing possible bias and contamination. Additionally, the mixed model enables use of information from all observations without imputing missing observations (White et al. 2012; Twisk et al. 2013). In terms of the intervention, the modified intervention mapping approach (Korshøj et al. 2012) is a strong feature, since the intervention is tailored specifically to the individual needs and wishes of the participating workplace and employees.

The generalizability of the findings is limited by the convenience sampling of only three companies in the area of Copenhagen, Denmark. The following significant ($p < 0.05$) differences were seen between those wanting to participate (consenters) and those not wanting to participate (non-consenters): the consenters had less job seniority and were more frequently born outside Denmark than the non-consenters. No differences were seen in diagnosed illnesses, level of occupational or leisure-time physical activity, gender, age, height, weight and job seniority. Overall, we consider the findings of the study to be generalizable. The cluster randomization was not accounted for in the sample size calculations. Another limitation of the study's results is missing observations. Observations are missing at random, which is accounted for by applying the mixed model, but also not at random due to exclusions from cardiorespiratory fitness testing. The number of participants dropping out between baseline and follow-up is not equally distributed between the intervention groups. In the aerobic exercise group, 19 participants were lost to follow-up, while in the reference group 15 participants were lost to follow-up (Korshøj et al. 2015). Given the small difference in the amount of participants lost to follow-up in the groups, we do not expect it to impact the results. The group lost to follow-up had a lipoprotein profile related to a higher cardiovascular risk at baseline than the population with completers, but more favourable levels of inflammation biomarkers. Those lost to follow-up would possibly therefore respond to the intervention differently to those not lost to follow-up, which means that the presented results could be skewed due to selection bias.

At the time of blood sampling, the participants were not fasting, and alcohol, tobacco and food consumption were not recorded before sampling, which could affect the levels of measured biomarkers and consequently the results. The half-life of HbA_{1c} (120 days) may be having an effect in this study, since the follow-up period of 4 months may be too short for evaluating the intervention effects. Changes in biomarkers reflect normal cyclical biological variations (e.g. diurnal and seasonal variations) (Hansen et al. 2007; Garde et al. 2000). Given that there was both a reference and an aerobic exercise group at each of the companies and that the baseline measurements were conducted at the three companies in January, August and September, we do not expect any bias from seasonal variation.

Additionally, we do not know whether the results are biased by psychosocial work environment due to lack of control by these factors. However, the cluster randomization is likely to minimize such potential bias.

Conclusion

This cluster-randomized study indicates that a worksite aerobic exercise intervention among cleaners leads to decreased levels of hsCRP and LDL cholesterol, and LDL/HDL and LDL/TC cholesterol ratios. Consequently, the aerobic exercise seems to improve inflammatory levels and lipoprotein profile among cleaners, with no signs of cardiovascular overload. Additional studies are needed to replicate these results in other blue-collar populations and to be able to make recommendations regarding physical exercise for workers with high levels of occupational physical activity.

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Compliance with Ethical Standards

Conflict of interest There are no competing interests.

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