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We know that leisure-time physical activity is related to reduced cardiovascular morbidity, but some recent papers provide evidence that physical activities at work are related to increased risk. We used job exposure matrices for assessment of physical activities at work, we found indications of slightly elevated long-term risks of acute myocardial infarction associated with lifting, but not with standing/walking.

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Acute myocardial infarction in relation to physical activities at work: a nationwide follow-up study based on job-exposure matrices

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Objective This study aimed to evaluate sex-specific risks of acute myocardial infarction (AMI) according to lifting and standing/walking at work.

Methods The study population included 1.15 million Danish wage earners. Annual job codes from 1976 onwards were linked to specific exposures using job-exposure matrices (JEM). Cases of AMI during follow-up 1996–2016 were retrieved from national registers. Incidence rate ratios (IRR) were computed by Poisson regression adjusting for demographic and JEM-assessed lifestyle factors. Models addressed physical activities at work the previous 0–2 years (short-term risk) and cumulative physical activities (long-term risk).

Results During 21.4 million person-years of follow-up, 22 037 AMI occurred in men and 6942 in women. Exposure–response relationships between recent physical activities at work and AMI were not evident. In men, the fully adjusted long-term IRR for the highest of five exposure categories compared to the lowest were 1.09 [95% confidence interval (CI) 1.03–1.15] for lifting and 1.01 (95% CI 0.96–1.07) for standing/walking. In women, the corresponding figures were 1.27 (95% CI 1.15–1.40) and 1.18 (95% CI 1.07–1.30). The latter risk estimate was strongly attenuated, and the trend became insignificant when adjusted for lifting. Findings were only partially supported by sensitivity analyses.

Conclusion The study provides limited support to the hypothesis that long-term lifting and standing/walking at work is related to increased risk of AMI. Possible effects of acute physical exertion are not addressed and bias towards the null because of crude exposure assignment cannot be ruled out.

Key terms cohort study; epidemiology; heart disease; heavy lifting; JEM; occupation; standing; strenuous work; walking.

There is strong epidemiological evidence that leisure-time physical activity is related to reduced cardiovascular morbidity and mortality (1–3). The lower threshold for beneficial effects seems to be less than moderate-intensity physical activity, such as brisk walking (4). The US Department of Health and Human Services recommends ≥150 minutes a week of moderate-intensity aerobic physical activity or 75 minutes a week of vigorous-intensity physical activity (5). The seminal epidemiological studies of bus drivers and longshoremen from the 1950s and 60s indicate that physical activities at work are also beneficial for cardiovascular health (6–8). On the other hand, more recent studies have reported increased risk of ischaemic heart disease (IHD, atherosclerosis of the coronary arteries, the most prevalent type of cardiovascular morbidity) with increasing physical activities at work (9–14). Together with observations of increased all-cause mortality in studies addressing physically demanding work (15), the discrepancy between the beneficial effects of leisure-

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time physical activity (LTPA) and the seemingly unfavourable effects of physical activities at work has been labelled a paradox (16, 17). However, studies often combine different physical activities at work such as walking, lifting, carrying, climbing stairs, and digging (18–21), even though relations with IHD may differ across activities (16). Thus, the evidence on effects of physical activities at work is far from clear.

In most studies of physical activities at work, exposure assessment is based on self-report, which may result in inflated risk estimates due to recall bias or deflated risk estimates because of inaccurate and crude assessment of exposure. Vaguely defined physical activities and potential confounding by social and lifestyle factors have been emphasized as major limitations (17). Other issues are small study populations, low participation, short follow-up time, limited exposure contrast and selective reporting.

Some of the methodological limitations of most earlier studies may be addressed by use of job-exposure matrices (JEM) in nationwide register-based studies, even though this approach may introduce other limitations such as exposure misclassification and challenges in obtaining information on potential confounders – information which is available in some recent large prospective studies (15, 22). JEM provide individual exposure measures in a transparent and independent way and can be applied in large populations with time specific information on occupation (23). Recently, lifestyle JEM have also been introduced (24, 25). Besides being time- and cost-effective, JEM may in some situations provide less attenuated risk estimates than individual-based exposure assessment (26). Men and women share established risk factors for IHD (27) and therefore major sex-specific effects of physical activities at work are not expected. Nevertheless, analyses stratified by sex are justified to evaluate the consistency of findings. Acute myocardial infarction (AMI) is a prevalent manifestation of IHD with well-defined diagnostic criteria and was selected for this study to ensure high specificity of the outcome.

The aim of this study was to evaluate the hypothesis that the sex-specific incidence rate of AMI is increased by short-term and long-term (cumulative) exposure to higher levels of physical activities at work in terms of lifting and standing/walking. These activities were chosen to include generic occupational activities of physically demanding and less-demanding nature.

Methods

Design and population

We conducted a follow-up study of all Danish residents, who in 1995 at an age of 31–50 years were gainful wage earners with a valid job code according to the Danish version of the International Standard Classification of Occupations from 1988 (DISCO-88) (28). We requested a DISCO-88 code at baseline in 1995 at the digit 2 level or higher. Military employees were excluded. The study population was retrieved as a subset of the Danish Occupational Cohort with eXposure data (DOC*X) after permission from the Danish Data Protection Agency (P-2019-04) and from Statistics Denmark (P-707006). DOC*X is profiled in a separate paper (29).

Assessment of physical activities at work 1976–2015

Annual job codes. The DISCO-88 codes in the DOC*X are based on the Employment Classification Module (30, 31). These data mainly stem from public and private companies but are also retrieved from tax authorities and unemployment insurance funds. Various classification systems of occupational titles have been used within the past decades. In the DOC*X, occupational codes according to other classification systems than DISCO-88 have been converted to DISCO-88 codes (29), which have been validated against self-reported information on job titles (32).

Expert-rated JEM on lifting. To obtain estimates of occupational lifting, we used The Lower Body JEM (33), which provides estimates of total load lifted (kg/day) at work. This JEM has documented predictive validity for several outcomes (34–37). The JEM was constructed by grouping 2227 occupational titles into 122 job groups that were considered homogeneous with respect to physical activities at work (121 exposed groups and 1 minimally exposed group). Five experts in occupational medicine independently assessed the average total load lifted per day. If the most detailed DISCO-88 code included occupational titles from different job groups, the average exposure was used with few exceptions (38). In Denmark, specialists in occupational medicine have vast experience in quantifying total load lifted during a working day in all types of occupations because compensation for low back disorders and hip osteoarthritis is based upon detailed documentation of lifting work. The mean weighted kappa statistic for interrater agreement on ranking of the 121 job groups was 0.49 (moderate agreement (32). With few exceptions, two external experts confirmed the face validity of the rankings of the mean values (32). Furthermore, the average score on time spent lifting obtained for 125 DISCO-88 codes among men and women in a population survey (39) was strongly predicted by ranking of job codes according the expert-rated JEM (supplementary material, www.sjweh.fi/show_abstract.php?abstract_id=3862, figure S1). The range across lowest and highest deciles of DISCO-88 codes was 80–2640 kg/day. The JEM is not sex- or age-specific.

Self-report JEM on standing/walking. To obtain sex- and age-specific exposure estimates for standing/walking, we used the Occupational Activity JEM (39), which provides a sum score for the time spent standing/walking during a working day. Data was derived from a questionnaire survey encompassing a population sample of employees in Denmark in 2012 (the Work Environment and Health in Denmark study, N=26 165, response proportion 51.5%). The question was: "Do you stand or walk at work?" With the following six response categories: (i) never, (ii) rarely, (iii) about ¼ of the time, (iv) about ½ of the time, (v) about ¾ of the time, and (vi) almost all the time. Each answer was assigned a score from 1 (lowest) to 6 (highest). Using best linear unbiased prediction modeling, sex- and age-specific scores were computed for 168 of the 372 DISCO-88 codes, where the survey provided enough information. For the purpose of this study, we computed average scores at the 2- and 3-digit level for codes without 4-digit level information. The intraclass correlation coefficient (ICC) across all 168 DISCO-88 codes was 0.42 for men and 0.44 for women. The range across lowest and highest deciles of DISCO-88 codes was 2.7–5.2 score points.

Exposure assignment by job-exposure matrices. Calendar-year specific exposures were assigned to each cohort member by linking DISCO-88 codes for the longest held job in a year with the JEM. For lifting, we assigned cumulative exposures corresponding to the pack-year concept of smoking. One ton-year was defined as lifting one ton per day for one year (38). For standing/walking, we assigned cumulative exposures by summing up the scores for each year. The cumulative exposures were calculated across calendar years from 1976 or age 20, whichever came first. If the DISCO-88 code was missing or indicated military employment in years with active employment status according to the Employment Classification Module (8.2%), we assigned the average individual exposure during the latest up to five years. If still missing, we assigned exposure estimates of zero. Years without employment were also assigned a zero value. The quantitative estimates of exposure intensities (kg/day and standing/walking score points) and cumulative exposures (ton-years and standing/walking sum scores) were categorized by the sex-specific 25th, 50th, 75th and 90th percentiles.

Outcome ascertainment

We excluded cohort members with any type of IHD before start of follow-up using data on hospital discharge diagnoses (ICD-8 codes 410 from 1977–1993; ICD-10 codes I21–I23 as principal diagnosis from 1994–2016) obtained from the Danish National Patient Register (31). The outcome in the follow-up period (1996–2016) only included the specific diagnosis of AMI (ICD-10 principal diagnosis I21) due to a high completeness of data and validity of hospital information on this disease. The positive predictive value of a first-time AMI diagnosis according to the Danish National Patient Register was 97% in a validation study using medical records as the gold standard (40). Data on prehospital deaths from AMI during follow-up was retrieved from the Danish Register of Causes of Death (40) and constituted 6.9% of all incident cases.

Covariates

From public registers hosted by Statistics Denmark, we obtained information on the following baseline variables (1995): sex (men/women) and highest education (primary, secondary, short tertiary, medium tertiary, long tertiary and missing) as well as the following annually measured time-varying variables: vital status (alive/dead), emigration (yes/no), disappearance (yes/no), age (integers), cohabitation (yes/no/missing), employment status [employee, employer, no gainful employment (including unemployment, long-term sick leave, disability pension and voluntary early retirement)] and social position defined by DISCO-88 major codes (first digit: 1–2 managers and professionals, 3 technicians, 4–5 clerks, service and sales workers, 6–7 skilled workers, 8–9 unskilled workers) (28).

Time-varying individual proxies of lifestyle factors in terms of sex-, age- and period-specific probability of current smoking and estimates of body mass index (BMI) (kg/m^2) and LTPA [score points low (1) to high (6)] were assigned by lifestyle JEM based on questionnaire information from several large random samples of the Danish population (24). Lifestyle exposures in years without employment and in years with missing DISCO-88 codes were assigned the individual average exposure during all previous years (10.9% and 8.2%, respectively).

Statistical analysis

We used Poisson regression to compute sex-specific incidence rate ratios (IRR) with 95% confidence intervals (CI) for the association between incident AMI and physical activities at work from start of follow-up 1 January 1996 until first-occurring incident AMI (including prehospital death from AMI), death of another cause, emigration, disappearance or end of follow-up 31.12. December 2016. P-values for monotonic trends across exposure categories were computed by assigning integer values 0–4 to exposure categories (excluding the missing category) and reported if $P<0.001$ or <0.05 (subset analyses). Data on education was missing in 19% of records. Missings were kept as a separate category in the analyses.

Short-term risk. We analyzed the incidence of AMI according to physical activities at work the previous calendar year. Since employment status could not be resolved in more detail than one year, the one-year time lag spanned one day and two years.

Long-term risk. We analyzed the incidence of AMI according to cumulative physical activities at work from 1976 until and including the previous year.

Adjustments. All models were adjusted by a fixed set of constant and time-varying covariates. The constant covariates included sex (by stratification) and highest education at baseline (6 levels including a category of missing). The time varying variables were age (integers), cohabitation (yes/no/missing), social position (DISCO-88 major groups, 6 levels including a category of missing), employment status (employee, employer, no gainful employment), smoking (25th, 50th, 75th and 90th percentiles), BMI (25th, 50th, 75th and 90th percentiles) and LTPA (25, 50, 75 and 90 percentiles). The grouping of the three lifestyle variables were based upon cumulative years with a probability above the upper quartile. All time-varying variables were analyzed with a one-year time lag.

Sensitivity analyses. First, to counteract potential attenuation of risk estimates by the correlation between number of exposed years and staying in employment because of good health (healthy worker survivor selection), we repeated the analysis of long-term risk but redefined cumulative exposure as exposure from 1976 until but not including 1996 (start of follow-up) and ignored exposure during subsequent years. Second, we performed analyses according to cumulative exposures during the ten most recent years based on the assumption that physical activities at work more than ten years ago have little impact, if any. Third, we calculated IRR within selected DISCO-88 major groups with large ranges of physical activities as an alternative way to account for potential confounding by social factors. Fourth, we repeated the analyses of short-term effects using models with adjustment for cumulative exposure accrued before the previous calendar year. Finally, we adjusted analyses of long-term standing/walking for effect of lifting.

Supplementary analyses. To examine potential interactions between lifting and the strong risk factors for AMI, smoking and BMI, we performed sex-stratified crude and fully adjusted analyses using models that in addition to main effects as continuous variables also included the product of cumulative lifting and (i) cumulative smoking and (ii) years with BMI in the upper tertile. All analyses were carried out in SAS 9.4 (SAS Institute, Cary, NC, USA) on a platform at Statistics Denmark.

Results

The study population included 1.15 million individuals with 41.5 million person-years equally divided in years before and after start of follow-up. The number of prehospital deaths due to AMI during follow-up and incident hospitalizations for AMI was 22 037 among men and 6 942 among women. A skewed distribution according to lifting was evident for highest education and social position, and for smoking, BMI and LTPA (table 1). All covariates – except LTPA – exhibited robust prospective and mutually independent associations with AMI in the expected direction (supplementary table S1). LTPA was, as expected, associated with reduced risk of AMI in analyses only adjusting for age, but not in fully adjusted analyses (table S1).

Lifting at work

Among men, the short-term risk of AMI was not associated with lifting (table 2). The fully adjusted long-term risk increased with increasing cumulative lifting (ton-years) up to the previous year reaching a maximum IRR of 1.09 (table 2). The associations were attenuated or disappeared in models using cumulative exposure before start of follow-up, in models based on the most recent ten years (supplementary table S2), and in three of four social strata with large ranges of cumulative lifting up to the previous year (see supplementary tables S3 for exposure ranges and S4 for results).

Among women, the fully adjusted short-term risk of AMI tended to increase with increasing lifting exposure reaching a maximum IRR of 1.16 (table 2), even when adjusted for cumulative lifting accrued before the previous calendar year (results not shown). The fully adjusted long-term risk increased with increasing cumulative lifting (ton-years) up to the previous year. Associations were also seen in sensitivity analyses only including cumulative exposure before start of follow-up (table S2), but not in models based on the previous ten years (table S2). Moreover, indications of higher risk with higher levels of exposure (intensity times duration) were seen in two of four social strata with large ranges of cumulative lifting up to the previous year (see table S3 for exposure ranges and table S4 for results), but tests for trend were not significant at the 5% level in any of these analyses (table S4).

There were no indications of an increased risk of AMI due to interaction between cumulative lifting and cumulative smoking in either sex in fully adjusted models (OR 1.00, 95% CI 0.99–1.01 in men; OR 1.01, 95% CI 0.99–1.02 in women). Corresponding figures for interaction between cumulative lifting and cumulative BMI were OR 0.99, 95% CI 0.99–1.00, for men and OR 0.98, 95% CI 0.97–1.00, for women.

Table 1. Characteristics of the study population at baseline (1995) and distribution of person-years according to total load lifted per day before and after start of follow-up on 1 January 1996. Lifting assigned by an expert-based job-exposure matrix (JEM). [LTPA=leisure-time physical activity.]

	Persons (N=1 115 413)		Person years (N=41 505 028)			
			Lifting in years before start follow-up (1976–1995, person years=20 138 845)		Lifting in at-risk years during follow-up (1996–2016, person years=21 366 283)	
	N	%	≤1000/500 kg/day [a] (N=16 679 084) %	>1000/500 kg/day [a] (N=3 459 761) %	≤1000/500 kg/day [a] (N=16 679 084) %	>1000/500 kg/day [a] (N=3 459 761) %
Sex						
Male	546 085	49.0	48.2	52.0	51.3	50.0
Female	569 328	51.0	51.8	48.0	48.7	50.0
Age (years)						
20–30	0	0.0	39.1	40.2	0	0
31–40	554 376	49.7	42.8	42.5	11.7	12.0
41–50	561 037	50.3	15.7	14.7	36.7	37.7
51–60	0	0.0	2.4	2.6	40.8	40.3
61–65	0	0.0	0.0	0.0	10.8	10.0
Cohabitation						
Yes	234 825	78.4	41.8	42.7	74.5	74.3
No	874 743	21.1	12.8	12.3	21.6	22.2
Missing	5 845	0.5	45.4	45.0	3.9	3.5
Highest education						
Long tertiary	65 318	5.8	4.7	0.2	8.2	0.1
Medium tertiary	180 237	16.2	15.4	1.9	21.9	1.7
Short tertiary	40 885	3.7	3.5	0.7	5.0	1.0
Secondary	424 584	38.1	35.1	32.0	39.4	54.0
Missing	191 608	17.1	24.3	31.6	8.6	11.2
Employment status [b]						
Employee	1 115 413	100.0	92.3	94.5	80.9	83.1
Employer	0	0.0	2.1	2.3	2.7	2.4
No gainful employment	0	0.0	5.6	3.2	16.4	14.6
Social position [b]						
Managers and professionals	217 972	19.5	18.2	0.8	25.4	1.5
Technicians	237 945	21.3	18.3	2.6	25.5	3.1
Clerks, service and sales workers	328 452	29.5	29.1	33.3	20.9	36.3
Skilled workers	141 618	12.7	13.1	19.4	8.7	14.9
Unskilled workers	189 426	17.0	13.3	37.3	10.7	33.5
Missing	0	0	8.0	6.7	8.7	10.5
Probability of smoking >Q3 [c] (men 0.57; women 0.52)						
Yes	241 395	21.6	42.4	60.0	4.4	16.7
No	874 018	78.4	53.2	36.4	95.6	83.3
Missing [d]	0	0	4.4	3.6	0	0
Probability of body mass index >Q3 [c] (men 25.4 kg/m^2; women 23.7 kg/m^2)						
Yes	247 844	22.2	11.4	26.3	26.5	40.3
No	867 659	77.8	84.2	70.1	73.0	59.7
Missing [d]	0	0	4.4	3.6	0	0
Probability of LTPA score >Q3 [c] (range 1–6; men 2.4; women 2.3)						
Yes	313 457	28.1	37.0	40.8	20.6	28.3
No	801 956	71.9	58.6	55.6	79.4	71.7
Missing [d]	0	0	4.4	3.6	0	0

[a] Median lifting 1976–2015 ≤ or >1000 kg/day for men and ≤ or >500 kg for women.
[b] No missing values before start of follow-up because of the inclusion criterion of a valid DISCO-88 code at baseline.
[c] Q3: 75th-percentile for the distribution of sex-, age- and period-specific JEM-based probability in 1995. Missing values in a year replaced by the individual average across all previous years.
[d] The sex-, age- and period-specific lifestyle JEM was incomplete for the period 1976–1994.

Standing/walking at work

Among men, the fully adjusted models did not consistently indicate associations between standing/walking at work and short- or long-term risk of AMI (table 3 and table S2).

Among women, there were no indications of increased short-term risks (table 3). The fully adjusted long-term risk increased with increasing cumulative standing/walking up to the previous year (reaching a maximum IRR of 1.18), but the association was attenuated when adjusting for long-term lifting (maximum IRR 1.11, 95% CI 1.00–1.23) and the trend became insignificant (P=0.08). Moreover, this relationship was neither found in models only including cumulative exposure before start of follow-up nor in models based on the previous ten years (table S2).

Table 2. Short- and long-term risk of acute myocardial infarction (AMI) according to lifting at work assessed by an expert-rated job-exposure matrix (JEM) [a]. **Bold indicates P-value for trend <0.001** (fully adjusted analyses only). [IRR=incidence rate ratios; CI=confidence intervals.]

Lifting at work	Men				Women				
	Cases	IRR [b]	IRR_{adj} [c]	95% CI	Lifting at work	Cases	IRR [b]	IRR_{adj} [c]	95% CI
Total load lifted per day the previous year, kg/day									
0	9859	1.00	1.00		0	4 488	1.00	**1.00**	
>0–100	417	0.96	**1.13**	1.02–1.25	>0–390	36	1.34	**1.12**	0.80–1.57
>100–620	5316	1.10	1.03	0.98–1.07	>390–1050	1 753	1.21	**1.14**	1.06–1.22
>620–1680	3529	1.16	1.04	0.99–1.09	>1050–3500	180	1.33	**1.16**	0.97–1.32
>1680–3500	2068	1.19	1.00	0.94–1.05	Missing	176	0.96	**1.07**	0.92–1.25
Missing	848	1.04	1.01	0.94–1.09					
Ton-years (1976 to previous year)									
0–≤3.1	4309	1.00	**1.00**		0–0.5	1 392	1.00	**1.00**	
>3.1–11.7	4770	1.25	**1.06**	1.01–1.11	>0.5–1.5	1 374	1.13	**1.06**	0.98–1.15
>11.7–25.6	5986	1.43	**1.08**	1.03–1.14	>5.1–12.4	1 707	1.38	**1.13**	1.05–1.23
>25.6–45.2	3353	1.50	**1.09**	1.03–1.15	>12.4–22.0	1 357	1.66	**1.22**	1.12–1.34
>45.2–126.6	3619	1.54	**1.09**	1.03–1.15	>22.0–118.0	1 112	1.71	**1.27**	1.15–1.40

[a] Lifting intensity (total load lifted per day) the previous calendar year and cumulative lifting (ton-years) assigned by an expert-rated JEM. Values grouped by the sex-specific 25th, 50th, 75th and 90th percentiles across all person-years.
[b] Adjusted for age (integers).
[c] Additionally adjusted for age (integers), cohabitation, highest education, employment status, social position, smoking, body mass index and leisure-time physical activity.

Table 3. Short- and long-term risk of acute myocardial infarction (AMI) according to standing/walking at work assessed by a self-report job–exposure matrix (JEM) [a]. **Bold indicates P-value for trend <0.001** (fully adjusted analyses only). [IRR=incidence rate ratios; CI=confidence intervals.]

Standing/walking at work	Men				Women				
	Cases	IRR [b]	IRR_{adj} [c]	95% CI	Standing/walking at work	Cases	IRR [b]	IRR_{adj} [c]	95% CI
Standing/walking per day the previous year, score									
1–≤2.8	5612	1.00	1.00		1–2.7	2273	1.00	1.00	
>2.8–3.5	3826	1.02	1.01	0.95–1.08	>2.7–3.6	1262	0.96	0.98	0.84–1.14
>3.5–4.7	4198	1.18	1.06	1.00–1.14	>3.6–4.8	1086	0.97	0.96	0.82–1.12
>4.7–5.1	3449	1.29	0.97	0.90–1.04	>4.8–5.1	991	1.17	1.04	0.89–1.22
>5.1–6.0	2058	1.14	0.90	0.83–0.97	>5.1–5.8	825	1.50	1.08	0.92–1.27
Missing	2894	1.10	0.94	0.87–1.00	Missing	505	1.04	0.91	0.77–1.08
Standing/walking sum score (1976 to previous year)									
1–≤ 60	3999	1.00	1.00		1–≤64.6	1277	1.00	**1.00**	
>60–85	4803	1.05	1.04	1.00–1.08	>64.6–86.9	1536	0.98	**1.03**	0.95–1.11
>85–111	5865	1.08	1.03	0.99–1.08	>86.9–113.2	1801	0.97	**1.05**	0.98–1.14
>111–136	4348	1.12	**1.06**	1.01–1.11	>113.2–138.4	1312	0.99	**1.10**	1.01–1.20
>136–229	3022	1.00	1.01	0.96–1.07	>138.4–228.6	1016	0.95	**1.18**	1.07–1.30

[a] Standing/walking at work according to a self-report JEM (Do you stand or walk? Never (1), rarely (2), about ¼ of the time (3), about ½ of the time (4), about ¾ of the time (5), almost all the time (6)). Values grouped by the sex-specific 25th, 50th, 75th and 90th percentiles.
[b] Adjusted for age (integers).
[c] Additionally adjusted for age (integers), cohabitation, highest education, employment status, social position, smoking, body mass index and leisure-time physical activity.

Discussion

In this register-based nationwide follow-up study using JEM for assessment of physical activities, we found indications of slightly elevated long-term risks of AMI associated with lifting at work, while no consistent associations were observed for standing/walking.

Strengths of the study are the large study population covering the entire spectrum of occupations, a follow-up period of 20 years, almost complete data, assessment of occupational and cardiovascular risk factors from young age, assignment of independent information on specific physical activities at work, reliable outcome ascertainment, comprehensive adjustment for social factors, adjustment for smoking, BMI and LTPA and statistical power to perform sex-specific analyses and analyses stratified by social position.

Limitations are primarily related to exposure misclassification, lack of detailed information on LTPA, residual confounding and the potential for a healthy worker survivor effect. Exposure assignment based on JEM inherently causes misclassification – let alone because a JEM does not reflect variation in exposure among individuals in the same occupations. As the within-occupation variation relative to the between-occupation variation increases, still larger study populations will be needed to separate true effects from statistical noise (41). The implication of exposure misclassification is inability to detect effects of the entire range of individual exposures, but risk estimates of the occurring average exposure across occupations are not expected to be attenuated. Since the ranges of job specific average exposures to lifting and standing/walking were rather wide, the study provides valuable information. However, risks related to the very high end of exposures – for instance lifting ≥10 tons/day – cannot be evaluated in this study since the highest JEM-based average lifting for an occupation was 3.5 tons/day. Further evidence regarding the validity of the JEM is the rather strong crude exposure–outcome associations in the expected direction observed in this study and the ability to predict several other outcomes in earlier studies (34–37).

The standing/walking JEM does not distinguish between standing and walking. We cannot exclude the possibility that prolonged standing is associated with an increased risk and walking without prolonged standing with a decreased risk resulting in no-risk when combined as in our study. However, to the best of our knowledge, there are no data to indicate that standing at work is a risk factor for AMI. Of note, a recent study included standing (shop assistants, security guards) in physical activities in parallel with lifting and leisure time physical activities and reported no increase in cardiovascular mortality (42). The design does not allow for examination of immediate (triggering) effects since the most detailed exposure resolution is one calendar year. For instance, it might be hypothesized that an acute severe exertion of heavy lifting at work might trigger AMI. This might be explored in future case-cross over studies. On the other hand, earlier epidemiological evidence is based upon the hypothesis that (unspecified) physical activities at work result in gradual cumulative damage to the cardiovascular system (16).

Residual confounding. The study benefits from sufficient statistical power to enable comprehensive adjustment for a range of well-established risk factors which all except LTPA independently predicted the risk of AMI. In many analyses, risks related to physical activities were strongly attenuated towards null in fully adjusted models. Socio-economic position is a strong risk factor of AMI and was accounted for by highest education, employment status and social position (DISCO-88 first digit groups) – and by analyses restricted to selected social strata with wide ranges of exposure. We did not have data on individual cardiovascular risk factors except that we were able to exclude persons who had been hospitalized due to IHD before start of follow-up. However, the use of lifestyle JEM for smoking and BMI performed well. Both factors were robustly and independently associated with AMI risk in both men and women, even after adjustment for highest education, social position and employment status. This adds to the evidence that these sex-, age-, and period-specific lifestyle JEM are valuable tools to adjust for risks related to lifestyle in register-studies without access to individual information (24).

However, the LTPA JEM did not consistently predict a reduced risk of AMI. This is perhaps not surprising since LTPA is prevalent regardless of type of occupation and low and high levels of LTPA occur in all job groups. . Nevertheless, this JEM serves the purpose of controlling confounding since exposure is also defined by JEM.

Other potentially confounding factors, such as heredity, hypertension, hyperlipidemia, diabetes, major depression (27), job strain (22), environmental (43) and occupational noise (44), shift work (45) and airborne particulate exposure (46), were not explicitly controlled for. Therefore, we are not able to exclude the possibility of residual confounding.

Healthy worker survivor effect. Individuals with emerging cardiovascular disease may leave physically demanding jobs long before death or hospitalisation for AMI leading to a healthy worker survivor effect (bias towards the null). This was probably counteracted by analyses only based upon exposure before start of follow-up, where cohort members were 30-50 years old and by including employment status as a covariate during follow-up.

Earlier findings

Although an increasing number of studies have addressed cardiovascular morbidity in relation to physical activities at work, direct comparisons of results are impeded by vaguely defined exposures. With few exceptions (21, 47), earlier studies relied on individual self-report of physical activities at one point in time and often combined various activities into one measure (9, 12–14, 19, 48). For example, one study defined physical activity as "standing and walking most of the time with quite a bit of carrying or lifting heavy burdens or work that requires vigorous or strenuous physical activity" (12) and another study defined physical activity as "most of the time you walk, and you often have to walk upstairs and lift various items (eg, mail delivery and construction work). Or you have heavy physical work. You carry heavy burdens and carry out physically strenuous work (eg, digging and shoveling)" (9). A Finnish study used a more transparent approach by converting self-report data on time spent in various activities into energy requirements (kcal/kg/hour) of these activities (sitting, standing, walking, climbing stairs – but without a category for heavier work) (13). Thus, the inability to distinguish more physically demanding work is a limitation of most previous studies. Moreover, confounding by individual and social risk factors is likely in many studies (17).

Sex differences. While most earlier studies reported effects in men (9, 12, 13, 19, 48), this study found most consistent associations in women. Biologically, it does not seem plausible that women are more susceptible to physical activities at work than men. The existence of sex-specific differences in the pathophysiology and pathogenesis of AMI is widely acknowledged (49) and some risk factors are more potent in women. However, men and women share all established risk/protective factors such as smoking, high BMI, exercise, diabetes, hypertension, and depression (27). It is therefore hard to figure out why physical activities at work would be deleterious in one sex but not in the other. In this study, we performed sex-stratified analysis to demonstrate consistency. It also seems unlikely that occupational exposure patterns and levels would confer a higher risk among women. However, the level of physical activity relative to the individual maximal capacity rather than the absolute level may be of importance (13). If women with physically demanding work have a higher work load relative to their maximal physical capacity than men, this might in fact explain sex differences, but this potential explanation of our findings seems less likely given the fact that we used lower category boundaries for lifting for women than for men. Of note, a large study of nurses with long follow-up found increased rate of incident IHD with increasing level of self-reported physical activities at work across all strata of self-reported LTPA (14). In this study physical activities were categorized as mainly sedentary (low), standing/walking (medium) and lifting/carrying/ heavy/fast/physically exerting work (high) (14).

Leisure time physical activity versus physical activities at work. It has been argued that the intensity of physical activity at work is too low to improve cardiorespiratory fitness and cardiovascular health (16). But this seems not to fit with evidence that even moderate physical activity such as brisk walking for 2.5 hours/week is related to substantially decreased cardiovascular mortality and that vigorous frequent physical training only accomplishes moderate additional risk reduction (4, 5). However, physical activity at work is distinguished by other characteristics. It has been argued that physical activity at work is associated with an elevation of the 24-hour heart rate and blood pressure (which is related to increased cardiovascular disease risk), insufficient recovery and work control and increased level of low-grade inflammation (16). Studies based on objective recordings of LTPA and specific physical activities at work are needed to corroborate or refute the relevance of these factors.

Concluding remarks

This study provides limited support to the hypothesis that long-term lifting and standing/walking at work are related to an increased risk of AMI.

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