Job Strain and Risk of Acute Recurrent Coronary Heart Disease Events

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Context There is evidence that job strain increases the risk of a first coronary heart disease (CHD) event. However, little is known about its association with the risk of recurrent CHD events after a first myocardial infarction (MI).

Objective To determine whether job strain increases the risk of recurrent CHD events.

Design, Setting, and Patients Prospective cohort study of 972 men and women aged 35 to 59 years who returned to work after a first MI and were then followed up between February 10, 1996, and June 22, 2005. Patients were interviewed at baseline (on average, 6 weeks after their return to work), then after 2 and 6 years subsequently. Job strain, a combination of high psychological demands and low decision latitude, was evaluated in 4 quadrants: high strain (high demands and low latitude), active (high demands and high latitude), passive (low demands and low latitude), and low strain. A chronic job strain variable was constructed based on the first 2 interviews, and patients were divided into those exposed to high strain at both interviews and those unexposed to high strain at 1 or both interviews. The survival analyses were presented separately for 2 periods: before 2.2 years and at 2.2 years and beyond.

Main Outcome Measure The outcome was a composite of fatal CHD, nonfatal MI, and unstable angina.

Results The outcome was documented in 206 patients. In the unadjusted analysis, chronic job strain was associated with recurrent CHD in the second period after 2.2 years of follow-up (hazard ratio [HR], 2.20; 95% CI, 1.32-3.66; respective event rates for patients exposed and unexposed to chronic job strain, 6.18 and 2.81 per 100 person-years). Chronic job strain remained an independent predictor of recurrent CHD in a multivariate model adjusted for 26 potentially confounding factors (HR, 2.00; 95% CI, 1.08-3.72).

Conclusion Chronic job strain after a first MI was associated with an increased risk of recurrent CHD.

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IT HAS BEEN SHOWN IN SEVERAL[1-6] BUT not all studies[7-9] that job strain, a combination of high psychological demands and low decision latitude,[10] increases the risk of a first coronary heart disease (CHD) event. However, the association of job strain with the risk of recurrent CHD events after a first myocardial infarction (MI) has been documented in only 2 prospective studies whose findings were inconsistent.[11,12] Two major limitations of these previous studies were that they did not assess the duration of psychosocial work exposure[11-13] and were conducted with a limited number of participants (n=62,[11] n=200[12]). Our study was undertaken to determine whether job strain increases the risk of recurrent CHD events when the duration of psychosocial work exposure is taken into account in a large cohort who returned to work after a first recent MI.

METHODS

Patients and Data Collection

A total of 1191 patients younger than 60 years were recruited from 30 hospitals in the province of Quebec, Canada, between November 1995 and October 1997. Eligible patients had a first acute MI, held a paid job in the 12 months before their MI, and planned to return to work at least 10 hours per week within 18 months after their MI. The ethics board of each hospital approved the study. Written informed consent was obtained before hospital discharge. The final study population included 972 patients (FIGURE 1).

Medical information regarding the acute MI and past medical history was documented during the first hospitalization. Participants were interviewed 3 times by telephone: at baseline in 1996-1998, an average of 6 weeks after their return to work, 2.2 years later in 1998-2000, and after 6.9 years in 2003-2005. Validated questionnaires for the first 2 inter-

See also p 1693 and Patient Page.

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views focused on demographics, hospital readmission, physical and chemical exposures at work, psychosocial factors in and outside work, personality, and CHD risk factors. The third interview focused on cardiovascular and noncardiovascular hospital readmissions. A listing of hospital readmissions was compiled for each patient and used to search medical records throughout hospitals in Canada and abroad.

Hospital readmissions and causes of death were checked against 2 valid and reliable administrative databases: the hospital summary database for Quebec residents (MED-ECHO)[14,15] and the Quebec Institute of Statistics,[16,17] with agreement for 98.8% of recurrent CHD events. We searched medical charts and databases for recurrence data for those who did not participate in a second or third interview. The period between MI and the baseline interview was considered as immortal person-time[18] and excluded from the analyses.

Outcome

The outcome was the first recurrent CHD event among a composite of fatal CHD, nonfatal MI, and unstable angina. A cardiologist and a vascular specialist, who were blind to the patients' characteristics, adjudicated the first MI, and each subsequent cardiovascular outcome. An MI diagnosis[19] required an increase in cardiac enzymes with 1 of the following symptoms: ischemic chest pain, evolutionary ST-T segment changes, or new Q waves. The unstable angina diagnosis required hospitalization due to prolonged chest discomfort attributed to angina with either ischemic electrocardiographic changes or urgent coronary revascularization within 14 days of symptom onset.

Causes of death were ascertained with hospital charts, next-of-kin interviews, autopsy result, and death certificates. CHD deaths were defined by the *International Classification of Diseases, Ninth Revision*, codes 410-414 as underlying causes of death.

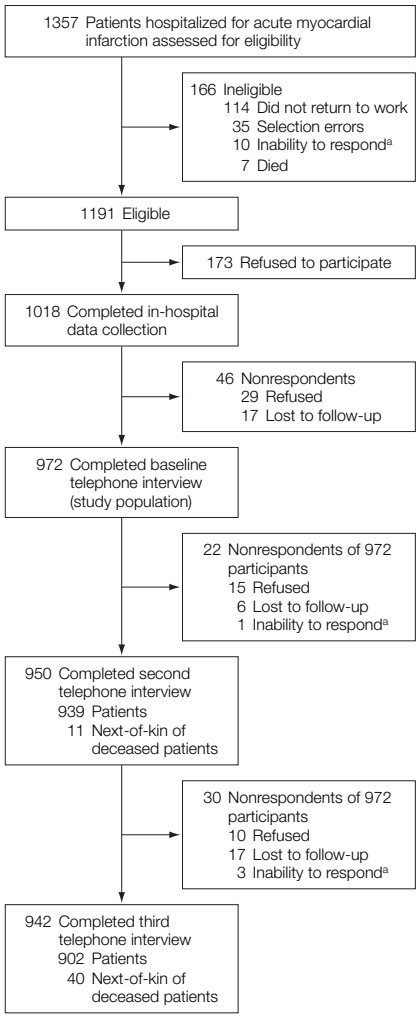
Job Strain

Psychological demands and decision latitude were assessed using the 18-item scale of the French validated version[20,21] of the Karasek Job Content Questionnaire.[22,23] Psychological demands refer to the quantity of work, intellectual requirements, and time constraints. Decision latitude refers to the possibility of making decisions, being creative, and using and developing one's abilities. Job strain was constructed by the combination of demands and latitude that were both dichotomized at the median of the distribution of a random sample of the general working population[21] and divided into 4 quadrants[23]: high strain (high demands and low latitude), active (high demands and high latitude), passive (low demands and low latitude), and low strain or reference (low demands and high latitude). With respect to baseline characteristics, job strain was also dichotomized into high strain vs non–high strain categories (after merging the active, passive, and low quadrants).

We hypothesized that the effects of exposure would persist during the first 6 months after the end of employment at a given job. Therefore, the psychosocial categories were imputed using information from the baseline interview for the 18 patients who at their second interview had ceased working for 6 months or less at their baseline job.

A 3-level variable of chronic job strain was constructed to assess the duration of exposure to high strain between baseline and the second interview: exposed to high strain at both interviews, unexposed or reference (the categories of nonhigh strain at either or both interviews were put together because of their similar rates), and stopped working for more than 6 months (separate category of 97 patients who had stopped working for more than 6 months before their second interview). Job strain quotient (demands/latitude),[24] and psychological demand and decision latitude scores were split into quartiles for analysis.

Figure 1. Flow Diagram



[a] Includes those who had language barriers or could not participate because they were too sick.

Other Measurements

The following classes of characteristics were assessed as potential confounders in multivariate models.

Sociodemographics: sex, age, marital status, education, perceived economic situation.

CHD risk factors: hypertension, dyslipidemia (treated or noted in medical record or diagnosed after first MI), diabetes mellitus, smoking status after MI, primary family members experiencing CHD younger than 60 years, and body mass index, obtained by self-report of height and weight.

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Table 1. Baseline Characteristics by Levels of Job Strain and Associations With Recurrent Coronary Heart Disease Events[a]

	No. (%)				
	Nonhigh Job Strain (n = 771)	High Job Strain (n = 201)	All Patients (N = 972)	Event Rate[b]	Hazard Ratio (95% CI)
Sociodemographics					
Sex					
Women	67 (8.7)	39 (19.4)	106	3.39	1 [Reference]
Men	704 (91.3)	162 (80.6)	866	3.62	1.07 (0.68-1.68)
Age, y					
≤39	76 (9.9)	25 (12.4)	101	4.91	1 [Reference]
40-49	351 (45.5)	94 (46.8)	445	3.46	0.71 (0.47-1.08)
50-59	344 (44.6)	82 (40.8)	426	3.44	0.71 (0.46-1.08)
Marital status					
Married/common law partner	651 (84.4)	159 (79.1)	810	3.62	1 [Reference]
Divorced/separated/widowed/single	120 (15.6)	42 (20.9)	162	3.47	0.95 (0.65-1.39)
Educational level					
College/university education	354 (45.9)	68 (33.8)	422	3.14	1 [Reference]
Primary/high school education	417 (54.1)	133 (66.2)	550	3.97	1.25 (0.95-1.66)
CHD risk factors					
Hypertension					
No	571 (74.1)	151 (75.1)	722	2.92	1 [Reference]
Treated	132 (17.1)	35 (17.4)	167	5.32	1.80 (1.29-2.50)
Untreated	68 (8.8)	15 (7.5)	83	6.63	2.25 (1.51-3.34)
Dyslipidemia					
No	271 (35.1)	64 (31.8)	335	1.45	1 [Reference]
Yes	500 (64.9)	137 (68.2)	637	4.87	3.31 (2.26-4.85)
Diabetes mellitus					
No	662 (85.9)	182 (90.5)	844	3.43	1 [Reference]
Yes	109 (14.1)	19 (9.5)	128	4.76	1.39 (0.97-2.00)
Smoking status					
Nonsmoker	87 (11.3)	16 (8.0)	103	3.29	1 [Reference]
Ex-smoker	482 (62.7)	116 (57.7)	598	2.87	0.88 (0.55-1.42)
Current smoker	200 (26.0)	69 (34.3)	269	5.57	1.69 (1.04-2.75)
Family history of CHD <60 y					
No	388 (50.3)	84 (41.8)	472	3.00	1 [Reference]
Yes	383 (49.7)	117 (58.2)	500	4.19	1.39 (1.05-1.83)
BMI, mean (SD)					
<30	623 (80.9)	156 (77.6)	779	3.38	1 [Reference]
≥30	147 (19.1)	45 (22.4)	192	4.45	1.31 (0.95-1.81)
Lifestyle factors					
Alcohol consumption per week, No. of drinks					
0	286 (37.1)	80 (39.8)	366	3.50	1 [Reference]
1-10	377 (48.9)	96 (47.8)	473	3.58	1.02 (0.76-1.38)
>10	108 (14.0)	25 (12.4)	133	3.90	1.12 (0.74-1.70)
Physical activity per week					
Vigorous	310 (40.2)	86 (42.8)	396	3.61	1 [Reference]
Moderate	335 (43.5)	67 (33.3)	402	3.33	0.92 (0.68-1.25)
Inactivity	126 (16.3)	48 (23.9)	174	4.25	1.17 (0.81-1.69)
Clinical prognostic factors					
Prior comorbid conditions[c]					
Angina[d]	79 (10.3)	22 (10.9)	101		
Percutaneous coronary intervention[d]	10 (1.3)	5 (2.5)	15		
Coronary artery bypass graft surgery[d]	6 (0.8)	2 (1.0)	8		
Stroke/transient ischemic attack[d]	8 (1.0)	3 (1.5)	11		
Peripheral vascular disease[d]	36 (4.7)	9 (4.5)	45		
COPD[d]	44 (5.7)	9 (4.5)	53		
Prior comorbid conditions, No.					
0	624 (80.9)	165 (82.1)	789	3.21	1 [Reference]
≥1	147 (19.1)	36 (17.9)	183	5.46	1.68 (1.23-2.30)
LVEF, %					
≥40	622 (90.4)	170 (90.9)	792	3.53	1 [Reference]
<40	66 (9.6)	17 (9.1)	83	4.22	1.19 (0.75-1.90)

(continued)

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Lifestyle factors: alcohol consumption; physical activity performed within the last 2 weeks evaluated in metabolic equivalent tasks–hours per week (METs-h/wk: 0 for inactivity, 0.25-14.08 for moderate, and >14.08 for vigorous exercise).[25]

Clinical prognostic factors: left ventricular ejection fraction (LVEF) less than 40%; number of prior comorbid

Table 1. Baseline Characteristics by Levels of Job Strain and Associations With Recurrent Coronary Heart Disease Events[a] (cont)

	No. (%)				
	Nonhigh Job Strain (n = 771)	High Job Strain (n = 201)	All Patients (N = 972)	Event Rate[b]	Hazard Ratio (95% CI)
Clinical prognostic factors (cont)					
Admission blood pressure, mean (SD), mm Hg					
Systolic	139.3 (27.1)	137.5 (26.0)			
Diastolic	84.5 (16.9)	83.4 (17.2)			
Hospital treatment and procedures					
No thrombolysis	355 (46.0)	88 (43.8)	443	3.21	1 [Reference]
Thrombolysis	416 (54.0)	113 (56.2)	529	3.94	1.23 (0.93-1.62)
Discharge medications[c]					
Antiplatelet agents[e]	715 (92.7)	184 (91.5)	899		
β-Blockers[e]	542 (70.3)	144 (71.6)	686		
Lipid-lowering agents[e]	405 (52.5)	106 (52.7)	511		
ACE inhibitors[e]	143 (18.5)	44 (21.9)	187		
Calcium channel blockers	105 (13.6)	36 (17.9)	141		
Discharge medications, No.					
≥3	347 (45.0)	93 (46.3)	440	3.96	1 [Reference]
2	313 (40.6)	81 (40.3)	394	3.47	0.88 (0.66-1.18)
1	98 (12.7)	23 (11.4)	121	2.53	0.64 (0.39-1.05)
0	13 (1.7)	4 (2.0)	17	5.74	1.41 (0.57-3.46)
Work environment					
Baseline social support at work					
High	360 (49.9)	51 (26.3)	411	4.26	1 [Reference]
Low	362 (50.1)	143 (73.7)	505	3.20	0.75 (0.57-0.99)
Chronic social support at work					
High	415 (58.0)	73 (38.8)	488	3.44	1 [Reference]
Low	226 (31.6)	92 (48.9)	318	3.37	0.98 (0.72-1.34)
Stopped working[f]	74 (10.4)	23 (12.2)	97	4.04	1.17 (0.74-1.85)
Physical and chemical factors, No.[g]					
0	180 (23.3)	29 (14.4)	209	2.87	1 [Reference]
1	161 (20.9)	25 (12.4)	186	3.69	1.28 (0.82-2.00)
2	163 (21.1)	38 (18.9)	201	4.75	1.64 (1.08-2.49)
≥3	267 (34.6)	109 (54.2)	376	3.38	1.17 (0.79-1.74)
Adverse work organization factors, No.					
0	93 (12.1)	32 (15.9)	125	3.26	1 [Reference]
1	365 (47.3)	106 (52.7)	471	2.89	0.89 (0.57-1.41)
2	222 (28.8)	45 (22.4)	267	4.33	1.32 (0.83-2.11)
≥3	91 (11.8)	18 (9.0)	109	5.44	1.66 (0.98-2.82)
Other factors					
Social support outside work					
High	610 (79.1)	148 (73.6)	758	3.44	1 [Reference]
Low	161 (20.9)	53 (26.4)	214	4.17	1.20 (0.88-1.65)
Psychological distress					
Low	548 (71.1)	117 (58.2)	665	3.31	1 [Reference]
High	223 (28.9)	84 (41.8)	307	4.25	1.27 (0.96-1.69)

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; CHD, coronary heart disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction.

[a] Denominator may vary due to missing information.

[b] Event rate per 100 person-years.

[c] Empty cells corresponded to variables not included individually in multivariate analyses but that were included in index variables (number of prior comorbid conditions, number of discharge medications).

[d] Comorbid conditions included in the number of prior comorbid conditions.

[e] Medication included in the number of discharge medications.

[f] Stopped working for more than 6 months before the second interview.

[g] Described in the "Methods" section.

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conditions (stroke, angina, coronary revascularization, chronic pulmonary disease); thrombolysis; number of in-hospital events during the first MI (reinfarction, recurrent angina, congestive heart failure, cardiac arrest, and coronary revascularization); and number of recommended medications after discharge.

Other work environment characteristics: social support at work assessed using four 5-item subscales of supervisor and coworker support and conflict from the validated Work Interpersonal Relationship Inventory.[26] The workers without a supervisor at baseline (n=178, 18.3%) and at the second interview (n=181, 18.6%) were imputed the double score of coworker support. A 2-level variable dichotomized at the median of the sample was used to measure baseline and chronic low social support at work between baseline and the second interview. The other variables were the number of physical and chemical exposures at work (passive smoking, chemicals, pollution, noise, excessive heat, excessive cold, and physical exertion at work); and the number of adverse work organization factors (absence of rest periods; owner, shareholder, or partner; seasonal job; self-employed; second paid job; 45-97 work hours per week and night work).

Other factors: social support outside work (low >0, high=0; range 0-11), using an 11-item subscale of the validated 19-item Medical Outcomes Study (MOS) Social Support Survey[27]; 3 personality factors with their scores split at the median (alexithymia,[28] hostile affect,[29] and suppressed anger[30]); and psychological distress (dichotomized at the highest quintile observed in the general population).[31,32]

Data Analyses

Person-years of follow-up were calculated from the baseline interview until the first recurrent CHD event, death, or the third interview, whichever came first. The third-interview nonrespondents were considered as dropouts and censored at the midpoint of the interval between the second and third interviews. Survival curves were obtained by the Kaplan-Meier method with log-rank test for comparison. Unadjusted rates of recurrent CHD per 100 person-years were computed. Cox regression models were used to estimate hazard ratios (HRs) of recurrent CHD and their 95% confidence intervals (CIs). The graphical check for parallelism between log-log curves suggested nonproportional hazards at approximately 2.2 years. The time axis partition revealed significant statistical interactions between job strain and each of these periods. Accordingly, all analyses were presented separately for the periods less than 2.2 and 2.2 or more years. Concerning chronic job strain, the study had respective statistical powers of 64% and 88% over the first and second periods to detect an HR of 2.0. All tests of significance ($P<.05$) were 2-tailed.

The model was first adjusted for each variable to test whether confounding changed the effect estimate by at least 5%. Variance inflation factors and condition indices revealed no multicollinearity between cofactors. Based on prior knowledge,[33-35] the modifying effects of sociodemographics and chronic low social support at work were analyzed with statistical interaction terms

Table 2. Unadjusted Hazard Ratios of Recurrent Coronary Heart Disease Events by Baseline Job Strain Components and Follow-up

Job Strain Components	Follow-up <2.2 y			Follow-up ≥2.2 y		
	No. (%) (N = 972)	Event Rate/100 Person-Years (No. of Events)	Unadjusted HR (95% CI)	No. (%) (n = 862)	Event Rate/100 Person-Years (No. of Events)	Unadjusted HR (95% CI)
Psychological demands at baseline, quartile (score range)[a]						
1 (12.0-20.6)	203 (20.9)	5.91 (24)	1 [Reference]	172 (20.0)	1.70 (13)	1 [Reference]
2 (21.0-23.0)	295 (30.4)	5.98 (36)	1.01 (0.60-1.70)	258 (29.9)	3.08 (34)	1.81 (0.95-3.42)
3 (23.1-26.0)	255 (26.2)	2.80 (15)	0.48 (0.25-0.91)	237 (27.5)	4.05 (40)	2.37 (1.27-4.42)
4 (27.0-36.0)	219 (22.5)	4.21 (19)	0.71 (0.39-1.30)	195 (22.6)	2.88 (25)	1.69 (0.87-3.31)
Decision latitude at baseline, quartile (score range)[b]						
4 (82.0-96.0)	219 (22.5)	4.39 (20)	1 [Reference]	197 (22.9)	2.60 (23)	1 [Reference]
3 (74.0-80.0)	230 (23.7)	4.23 (20)	0.96 (0.52-1.79)	205 (23.8)	3.16 (28)	1.21 (0.70-2.10)
2 (68.0-72.0)	261 (26.8)	6.75 (35)	1.53 (0.88-2.65)	220 (25.5)	2.88 (27)	1.11 (0.64-1.93)
1 (24.0-66.0)	262 (27.0)	3.46 (19)	0.79 (0.42-1.47)	240 (27.8)	3.34 (34)	1.29 (0.76-2.18)
Job strain at baseline						
Low strain	177 (18.2)	5.83 (21)	1 [Reference]	153 (17.7)	3.15 (21)	1 [Reference]
Passive	322 (33.1)	6.00 (39)	1.03 (0.60-1.75)	278 (32.3)	2.15 (26)	0.69 (0.39-1.22)
Active	272 (28.0)	3.35 (19)	0.58 (0.31-1.07)	249 (28.9)	2.71 (30)	0.86 (0.49-1.50)
High strain	201 (20.7)	3.59 (15)	0.62 (0.32-1.20)	182 (21.1)	4.69 (35)	1.48 (0.86-2.55)

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Nine-item scale of psychological demands of the Karasek Job Content Questionnaire (score range, 12.0-36.0).
[b] Nine-item scale of decision latitude from the Karasek Job Content Questionnaire (score range, 24.0-96.0).

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along with job strain ($P<.10$). The second-interview nonrespondents (n=22), the deceased (n=11), and the patients on long-term sick leave (n=10) were excluded from analysis of chronic job strain. We used dummy indicators for LVEF (n=97, 10%) and chronic social support at work (n=69, 7.1%) with missing information for more than 5% of the participants. Little missing information was otherwise observed: smoking status (n=2), body mass index (n=1), and suppressed anger (n=1). Second, the model was adjusted sequentially for each subgroup of cofactors to assess a possible overadjustment by mediators such as CHD risk factors and psychological distress. Third, the model was fully adjusted for fixed and time-dependent covariates. Time-dependent covariates were age, marital status, perceived economic situation, smoking status, body mass index, alcohol consumption, physical activity, number of recommended medications, number of adverse work organization factors, social support outside work, and psychological distress. Analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina).

RESULTS

The mean (SD) time to return to work after MI was 3.6 (2.4) months. During the mean follow-up of 5.9 years (median 6.7 years), 206 patients had a confirmed recurrent CHD event (111 nonfatal MI, 82 unstable angina, and 13 fatal CHD), for an overall recurrent rate of 3.60 per 100 person-years corresponding to a cumulative incidence of 21.2%. Of these 206 patients, 22 (10.7%) had a second recurrence, the first recurrence having occurred between the first MI and the baseline interview. The baseline characteristics of the 950 respondents and the 22 nonrespondents at the second interview were similar, except that the nonrespondents were more likely to be divorced, separated, or single; to be less educated; to have untreated hypertension, diabetes mellitus, and psychological distress; and to be heavy drinkers ($P\leq.05$).

Patients exposed to high strain differed from unexposed patients with respect to sex, education, smoking status, family history of premature CHD, physical activity, and social support at work ($P\leq.05$, TABLE 1). Cofactors such as CHD risk factors, number of prior comorbid conditions, 2 physical and chemical exposures at work, 3 or more adverse work organization factors and psychological distress increased the risks of recurrent CHD.

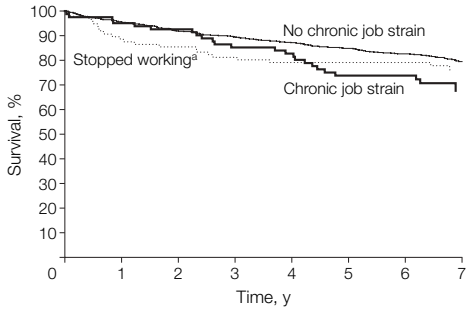
There was little association of baseline exposure to job strain components

Table 3. Adjusted Hazard Ratios of Recurrent Coronary Heart Disease Events by Baseline Job Strain Components and Follow-up

Job Strain Components (n = 971)	Adjusted HR (95% CI)[a] Follow-up <2.2 y	Follow-up ≥2.2 y
Psychological demands at baseline, quartile (score range)[b]		
1 (12.0-20.6)	1 [Reference]	1 [Reference]
2 (21.0-23.0)	0.99 (0.59-1.68)	1.77 (0.92-3.38)
3 (23.1-26.0)	0.43 (0.22-0.83)	2.25 (1.19-4.28)
4 (27.0-36.0)	0.67 (0.36-1.26)	1.59 (0.79-3.19)
Decision latitude at baseline, quartile (score range)[c]		
4 (82.0-96.0)	1 [Reference]	1 [Reference]
3 (74.0-80.0)	1.09 (0.58-2.05)	1.39 (0.79-2.45)
2 (68.0-72.0)	1.65 (0.93-2.92)	1.22 (0.68-2.16)
1 (24.0-66.0)	0.84 (0.44-1.61)	1.37 (0.79-2.40)
Job strain at baseline		
Low strain	1 [Reference]	1 [Reference]
Passive	1.04 (0.60-1.80)	0.68 (0.38-1.23)
Active	0.54 (0.29-1.03)	0.82 (0.46-1.45)
High strain	0.58 (0.29-1.16)	1.45 (0.82-2.58)

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Adjusted for 26 covariates, among which 15 were fixed (sex, education, hypertension, dyslipidemia, diabetes, family history of coronary heart disease <60 y, left ventricular ejection fraction, number of prior comorbid conditions, thrombolysis, number of in-hospital events, chronic social support at work, number of physical and chemical exposures at work, alexithymia, hostile affect, and suppressed anger) and 11 were time-dependent (age, marital status, perceived economic situation, smoking status, body mass index, alcohol consumption, physical activity, number of recommended medications, number of adverse work organization factors, social support outside work, and psychological distress).
[b] Nine-item scale of psychological demands of the Karasek Job Content Questionnaire (score range, 12.0-36.0).
[c] Nine-item scale of decision latitude from the Karasek Job Content Questionnaire (score range, 24.0-96.0).

Figure 2. Cumulative Incidence of Recurrent Coronary Heart Disease Events by Chronic Job Strain Among Patients After Myocardial Infarction



No. at Risk								
No chronic job strain	750	717	688	664	645	622	597	261
Chronic job strain	82	78	76	70	67	58	56	19
Stopped working[a]	97	86	83	77	74	71	69	36

Analysis excludes second interview of those classified as nonrespondents.
[a] Stopped working for more than 6 months before second interview.

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with risk of recurrent CHD except for the third quartile of psychological demands in the second period (TABLE 2 and TABLE 3).

However, chronic exposure to job strain was associated with an increased risk. Indeed, Kaplan-Meier curves showed lower survival rates for patients exposed to chronic job strain compared with those unexposed from 2.2 years to the end of follow-up (FIGURE 2). Chronic job strain was associated with a 2-fold increase in the unadjusted risk of recurrent CHD in the second period (TABLE 4). There were no significant statistical interactions between chronic job strain and either sex (*P*=.56), or age (*P*=.72), marital status (*P*=.71), education (*P*=.33), perceived economic situation (*P*=.75), and chronic low social support at work (*P*=.12).

Only dyslipidemia, smoking status, and number of adverse work organization factors were confounders that changed the effect estimate of chronic job strain by at least 5%. Chronic job strain remained associated with recurrent CHD in all sets of sequential adjustment (Table 4). Analysis using continuous values of chronic job strain (quotient) yielded positive results for the last quartile with an adjusted HR of 1.67 (95% CI, 0.95-2.94) in the second period.

Post hoc stratified analyses were carried out separately in patients with LVEF less than 40% to examine whether the association of job strain with recurrent CHD could be worse in this subgroup. Among the 80 patients with LVEF less than 40%, the HR of chronic job strain was 8.02 (95% CI, 1.99-32.32) in the second period. Among the 758 patients with LVEF of 40% or more, the HR of chronic job strain was 1.80 (95% CI, 1.00-3.26).

Table 4. Unadjusted and Adjusted Hazard Ratios of Recurrent Coronary Heart Disease by Chronic Job Strain and Follow-up[a]

	Chronic Job Strain, HR (95% CI)		
Model Adjusted for Cofactors, by Follow-up[b]	Unexposed (n = 750)[c]	Exposed (n = 82)[d]	Stopped Working >6 mo[e] (n = 97)
None			
<2.2 y	1 [Reference]	0.89 (0.38-2.05)	1.83 (1.03-3.27)
≥2.2 y	1 [Reference]	2.20 (1.32-3.66)	0.80 (0.39-1.66)
Sociodemographic factors			
<2.2 y	1 [Reference]	0.80 (0.34-1.86)	1.99 (1.10-3.60)
≥2.2 y	1 [Reference]	2.04 (1.22-3.41)	0.81 (0.39-1.69)
CHD risk factors			
<2.2 y	1 [Reference]	0.76 (0.33-1.76)	1.79 (1.00-3.22)
≥2.2 y	1 [Reference]	2.02 (1.21-3.37)	0.83 (0.40-1.72)
Lifestyle factors			
<2.2 y	1 [Reference]	0.87 (0.38-2.02)	1.86 (1.04-3.33)
≥2.2 y	1 [Reference]	2.21 (1.33-3.69)	0.81 (0.39-1.68)
Clinical prognostic factors			
<2.2 y	1 [Reference]	0.90 (0.39-2.07)	1.77 (0.99-3.17)
≥2.2 y	1 [Reference]	2.30 (1.37-3.84)	0.77 (0.37-1.60)
Work environment characteristics			
<2.2 y	1 [Reference]	0.92 (0.40-2.15)	1.88 (1.04-3.41)
≥2.2 y	1 [Reference]	2.31 (1.36-3.91)	0.88 (0.38-2.03)
Other factors			
<2.2 y	1 [Reference]	0.88 (0.38-2.05)	1.79 (1.00-3.21)
≥2.2 y	1 [Reference]	2.26 (1.35-3.80)	0.79 (0.38-1.62)
All cofactors			
<2.2 y	1 [Reference]	0.86 (0.36-2.03)	2.00 (1.08-3.72)
≥2.2 y	1 [Reference]	2.38 (1.37-4.13)	0.81 (0.34-1.90)

Abbreviations: CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction.
[a] Of the 929, 11died, 10 took long-term sick leave (> 1 year), and 22 did not respond.
[b] Each subgroup of cofactors is described in the "Methods" section.
[c] Unadjusted event rates for periods before 2.2 years is 3.94 and 2.81 at or beyond 2.2 years per 100 person-years.
[d] Unadjusted event rates for periods before 2.2 years is 3.49 and 6.18 at or beyond 2.2 years per 100 person-years.
[e] Stopped working for more than 6 months before the second interview. Unadjusted event rates for periods before 2.2 years is 7.28 and 2.27 at or beyond 2.2 years per 100 person-years.

COMMENT

Chronic job strain was associated with a significantly increased risk of recurrent CHD events from 2.2 years of follow-up and beyond among middle-aged patients who returned to work after a first MI. These results were obtained after full adjustment for 26 CHD-risk factors and sociodemographics, lifestyle, and clinical-prognostic and work-environment characteristics.

Our study has several strengths. This was a large prospective study of men and women with a high participation rate. Only first definite MI cases were included to avoid an eventual ascertainment bias.[36] Chronic effects of work characteristics were calculated taking into account changes between 2 time points. The time at risk for exposure to job strain was defined as starting at the baseline interview and lasting for the first 6 months of unemployment.[18] Several potential confounders, modifiers and mediators were measured and sequentially adjusted for in models to provide valid estimates. In general, the coronary risk profile and treatment were in line with expectations for a Canadian post-MI population in the mid-1990s with a preserved mean ejection fraction.[37,38] Results observed herein for traditional CHD risk factors follow the prognostic patterns found in previous population-based studies[39,40] and therefore support the validity of the data.

Our stratified analysis showed that the job strain effect may be extrapolated to middle-aged patients but was possibly worse for those with LVEF less than 40%. Another argument that supports the generalization to patients with LVEF less than 40% is that, in our population, the use of 2 evidence-based drugs such as angiotensin-converting enzyme inhibitor and angiotensin-receptor blocker (respectively, 65% and 58% at baseline and the second interview) was comparable with that found for such patients in the general population during the same period.[41]

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Our study has some limitations. Measurement error in job strain is possible. However, this misclassification would likely result in an underestimation of the true effect.[36,42] In addition, to avoid misclassification bias,[42] the 97 patients who had stopped working for more than 6 months before their second interview were analyzed separately because their risk was intermediate between those exposed to chronic job strain and those unexposed to high strain at one or both interviews. To gain statistical power, dummy indicators were created for ejection fraction and chronic low social support. Dummy indicators could yield confounded results if the variables were confounders leading to biased estimates of the overall effect.[18] Nevertheless, analysis with and without dummy indicators generated comparable effect estimates ensuring the validity of the results. A nonresponse bias may not significantly impact the results of chronic job strain since excluding the few nonrespondents at second interview (n=22, 2.3%) only slightly changed the baseline effect estimates of job strain.

Our study's findings should be considered in light of other studies. None of the 2 previous studies conducted on the current topic assessed duration of exposure. In the first study, job strain assessed at baseline was found to be an independent predictor of CHD mortality. However, the study was conducted in a small sample of 62 men of a limited age range (<45 years). In the second study, job strain assessed at baseline was not associated with recurrent CHD in a cohort of 200 women aged 55.8 years on average and followed up for a median of 4.8 years after an MI or an unstable angina.[12] Not assessing duration of exposure may generate an information bias, which could lead to an underestimation of the true effect.[18,35]

The results of the current study, showing an effect for chronic exposure while finding no effect for exposure assessed only at baseline, underline the importance of measuring exposure duration to provide valid effect estimates that take into account changes in exposure over time.[13] The 2-wave data measurement allowed us to assess for the first time the temporal relationship of job strain with recurrent CHD. The surprising lack of association of job strain that was observed during the first 2 years of greater vulnerability for patients after MI could be explained by the fact that a certain time lag is needed for job strain to have an effect as has been observed with other outcomes.[43,44]

High social support at work was not associated with reduced risk in this study. This is consistent with 2 previous studies that found that social support at work was not associated with cardiovascular risk[3,45] although one previous study did find an association with reduced risk.[46] The absence of an association could possibly be related to the specific situations involved. Indeed, receiving social support in "no problem" and "solvable problem" situations may not be associated with lower risk.[47]

The excess risk of recurrent CHD observed for the third quartile of psychological demands is not supported theoretically[10] nor empirically[35] and could reflect an artifact introduced by the categorization in quartiles.[48]

Several biologically plausible hypotheses may explain the independent association of chronic job strain with recurrent CHD. The first hypothesis is a direct effect of job strain via an increased activation of the sympathetic and the renin-angiotensin-aldosterone systems contributing most likely to an accentuated inflammation of the arterial wall and subsequently to the formation of thrombosis.[49-53] These findings are indirectly supported by the effects of job strain on heart rate variability.[49] It has also been shown that after an MI, there is a positive relationship between reduced heart variability, the autonomic nervous system activities and increased inflammatory markers.[50] The second hypothesis, which seems unlikely, is that there is an indirect effect of job strain on recurrent CHD, mediated by a lack of adherence to a healthier lifestyle and drug therapy.[54] Our data do not however support this hypothesis because the effect remained similar after adjustment for lifestyle and drug therapy.

This study found that chronic job strain significantly increased the risk of recurrent CHD among middle-aged patients who returned to work after a first MI. These results suggest that preventive interventions aimed at reducing job strain might have a significant impact on recurrent CHD events. Although further studies are required to establish optimal interventions, information about the results of this study should be disseminated in cardiac practice[55,56] and in occupational health services with the aim of reducing job strain for workers returning to work after an MI.

Author Contributions: Dr Aboa-Éboulé had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.
Study concept and design: Brisson, Maunsell, Bourbonnais, Vézina, Mâsse, Théroux, Dagenais.
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