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Original Article

Increased job strain and cardiovascular disease mortality: a prospective cohort study in U.S. workers

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Abstract: Job strain is considered a potential risk factor of cardiovascular disease (CVD). Our objective was to examine prospective associations of job strain with CVD mortality using data from the national, population-based Mid-life in the United States (MIDUS) cohort study, while considering changes in job strain. Job strain measure was based on Demand-Control model at Wave 1 in 1995–1996 and Wave 2 in 2004–2006, and CVD mortality data through 2018 were retrieved through linkage to the National Death Index (NDI). Cox proportional hazards regression was applied to assess prospective associations between job strain across MIDUS I and MIDUS II and CVD mortality at follow-up in 1,870 workers free from CVD at MIDUS I. After adjustment for relevant covariates, single measurement of job strain at MIDUS I or MIDUS II, and two measurements of job strain between the two waves were not significantly associated with CVD mortality, while the increase in scores between the two waves (increase vs. no increase) demonstrated stronger prospective associations with CVD mortality (HR and 95% CI = 2.37 [0.88, 6.42]). Our findings suggest increased job strain may pose a stronger risk to CVD mortality than single exposure measurement.

Key words: Job strain, Cardiovascular disease mortality, Changes, Cohort study

Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States (U.S.), incurring over 600,000 deaths and $320 billion in healthcare costs and productivity lossess[1)] annually, and with a prevalence nearing 50%[1–4)]. Job strain, defined as the combination of high job demand and low job control, has been found to be associated with an increased risk of CVD, with a series of systematic reviews and meta-analyses reporting links between high job strain and multiple CVD outcomes, including ischemic heart disease, cerebrovascular disease, peripheral artery disease, as well as CVD risk factors[5–12)].

However, much of the evidence relating job strain with CVD risk was generated in European countries[5, 8, 11, 13–15)], and there is a comparative lack of current data assessing associations of job strain with CVD risk in the U.S.—studies using data from U.S. populations are generally

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both inconsistent and dated[16–21], and there are no studies assessing changing exposures to job strain over time in the U.S., presenting an insular research gap.

Furthermore, psychosocial workplace exposures may be repeated or prolonged in nature, and much of the evidence base regarding job strain and CVD is founded on single baseline measures of job strain, which may result in exposure misclassification bias due to potential changes in job strain over time. This is a limitation that has been identified by previous studies of epidemiological and occupational health outcomes, highlighting a need for further studies employing triangulation, or the use of multiple methods of measurement in exposure assessment[14, 22–24]. Finally, there is a scarcity of evidence specifically investigating the effects of changes in job strain; one cohort study reported a reduction in HRV in nurses experiencing prolonged job strain over the course of one year[25], while a cohort of 10,308 British workers found a dose-response relationship between cumulative job strain and metabolic syndrome over the course of 14 yr[26]. Another population-based cohort study of employees in Denmark found that persistent job strain across a period of ten years was associated with an increased risk of incident CHD[14].

The aim of this study is to investigate associations of job strain with CVD mortality using prospective cohort data from the Mid-life in the United States (MIDUS) Study, with a national, population-based sample[27–29], providing evidence to fill this knowledge gap using recent data. To better clarify previous inconsistent findings regarding associations of job strain with CVD risk, we utilize multiple operationalizations of job strain, examining time specific associations (i.e., job strain measured at two time points), cumulative associations (i.e., mean job strain across two time points), and longitudinal associations (i.e., increases in job strain between two time points) using Cox proportional hazards regression. Hence, we hypothesize that these differential measures of job strain will lead to marked changes in observed associations of job strain with CVD, and that due to an analytical strategy that accounts for potential exposure misclassification bias, associations of increased job strain between two time points will indicate greater elevation of CVD risk than other measures of job strain.

Subjects and Methods

Study population

Data from the MIDUS I[27] and MIDUS II[28] surveys were used for this current research study. The MIDUS I study, initiated in 1995–1996, is a national longitudinal study that examines psychological, social, and behavioral factors and health among U.S. adults. The MIDUS II survey was carried out from 2004–2006, with mortality data through 2018 made available via additional linkage to the National Death Index (NDI). Data were collected via random digit dial (RDD) phone interviews and a self-administered questionnaire (SAQ). In total, 7,108 people participated in the MIDUS I study, with an overall response rate of 61%. The MIDUS II survey in 2004–2006 had 4,963 participants, representing a follow-up rate of 70%. Sources of retention and attrition between the MIDUS I and MIDUS II surveys were previously described elsewhere, with higher retention rates found among individuals with better health and higher educational attainment[30]. The sample for the current study was restricted to working people. In MIDUS I, 3,693 participants reported that they were working. In MIDUS II, 2,823 were followed up, and 1,919 were still working (accounting for 52% of working subjects in MIDUS I). We excluded 12 participants who had experienced a myocardial infarction (MI) or stroke event prior to MIDUS I, which were identified by an affirmative response to a disease checklist. We further excluded 37 participants who were missing data on job strain or covariates in MIDUS I and MIDUS II. Follow-up time was defined as starting at the beginning in the MIDUS I survey, and censoring of CVD death events occurred between MIDUS II and 2018. The final sample size for the current analysis consisted of 1,870 workers with complete data on two repeated measures of job strain at MIDUS I and MIDUS II surveys, and all of them were followed up through 2018 with vital information on death records (see below). The process of sample size selection is shown in Fig. 1. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines[31]. All participants provided written informed consent. This study was reviewed and approved for exemption by the University of California, Los Angeles Institutional Review Board (IRB#20-001044).

Measures

Job strain was defined using Karasek's Job Demand-Control model, the combination of high job demands with low job control[32]. In MIDUS I and MIDUS II, job demands were measured with 5 items, for example, "How often do you have to work intensively?", and "How often do you have a lot of interruption?". Job control was measured with 9 items, including 3-item skill discretion (items such as "How often do you learn new things at work?")

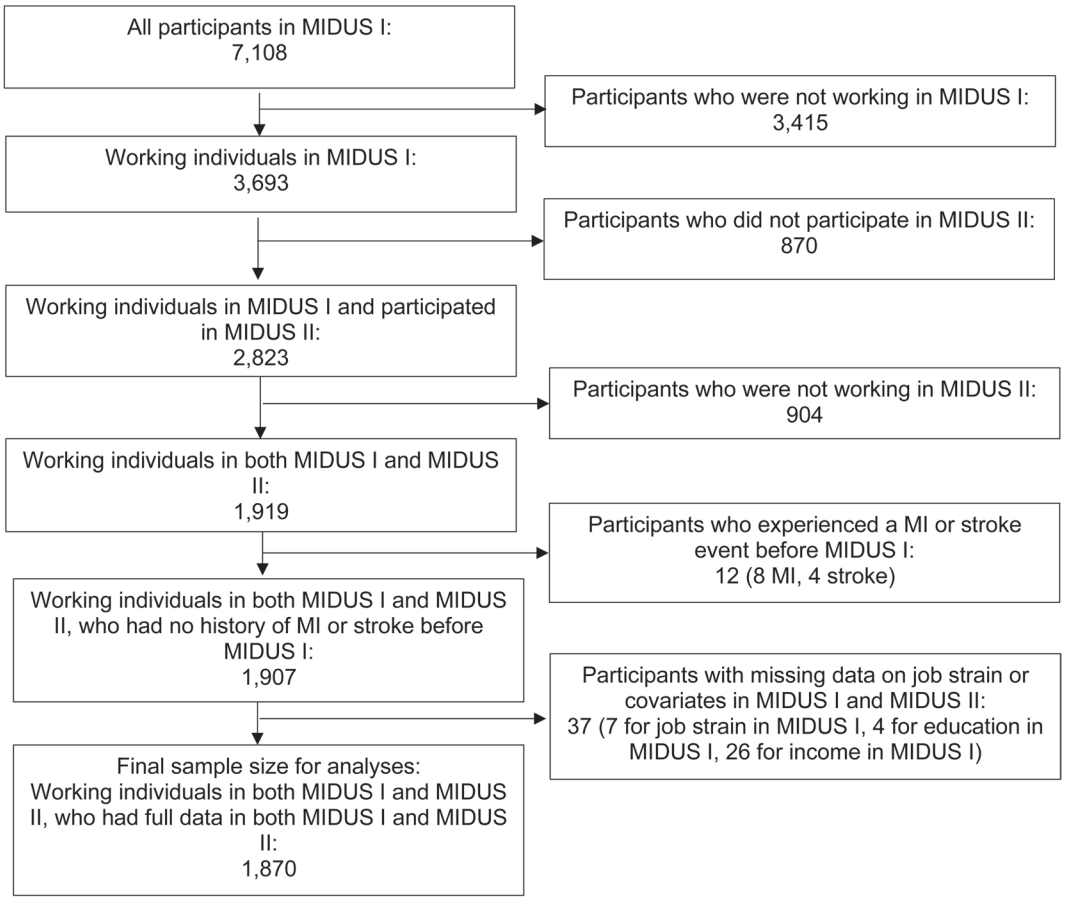

Fig. 1. Sample size selection.

and 6-item decision authority (example items were "How often do you have a choice in deciding how you do your tasks at work?", and "How often do you have a say in decisions about your work?"). Responses for job demands and job control were measured using a 5-point Likert scale (1=never, 5=all of the time). The questions for job demands and job control in the MIDUS study are comparable to those of the standard Job Content Questionnaire (JCQ) developed by Karasek (see Supplementary Table 1)[33], and have been used in prior analyses of the MIDUS study data[34]. Job demands and control were dichotomized into high and low levels by their median scores (16 and 33 in MIDUS I, and 15 and 33 in MIDUS II, respectively)[33], and binary job strain was thus defined as the combination of both high job demands and low job control.

CVD mortality data through 2018 were accessed via a separate dataset linked to the National Death Index (NDI) with variables specifying decedent status, source of decedent information, month and year of death, and International Classification of Diseases (ICD) codes[35]. Deaths that occurred due to CVD were identified using ICD-9 codes 390–459 and ICD-10 codes I00-I99. Sociodemographic factors at Wave 1 were included as covariates, including sex, age (<46; 46 to 55; and ≥56 yr old)[34, 36], race (White; Black; and Other), marital status (married; never married; and others), educational attainment (high school or less; some college; university or more), and household annual income (<$60,000; $60,000 to $99,999; ≥$100,000).

Statistical analysis

First, descriptive statistics were generated, and relative frequencies were examined for characteristics of the study sample. Second, the prospective associations of job strain with risk of CVD mortality were assessed using Cox proportional hazards regression, and the results were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). Multivariable regression models were calculated in two steps: Model I was adjusted for age and sex, and further adjustment for race, marital status, educational attainment, and household income was added in Model II. In order to account for possible exposure misclassification

bias due to changes in job strain in longitudinal design, we defined 4 sets of exposure assessment: (i) single job strain at MIDUS I only; (ii) single job strain at MIDUS II only; (iii) mean job strain across MIDUS I and MIDUS II; and (iv) increased job strain between MIDUS I and MIDUS II. We calculated mean sores of job demand and job control across MIDUS I and MIDUS II [(MIDUS I score + MIDUS II score)/2], identified the median points of mean job demand and job control, and then combined high mean job demand and low mean job control, resulting in a measure of mean job strain across MIDUS I and MIDUS II. To calculate increased job strain between MIDUS I and MIDUS II, we computed differences of job demand and job control between MIDUS I and MIDUS II (MIDUS II score − MIDUS I score) and identified individuals with increased job demand and decreased job control − participants exposed to combined increased job demand and decreased job control were classified as those with increased job strain between MIDUS I and MIDUS II. The process followed for constructing differing exposure models based on either one or two measurements of job strain are shown in Fig. 2. In order to address potential immortal time bias[37], all Cox proportional hazards regressions were conducted considering recourse of age as time scale and delayed entry age at the beginning of the study. In addition, we conducted sensitivity analyses with adjustment for the health behaviors of smoking, alcohol consumption, and physical exercise at MIDUS II to test their mediating role between job strain and CVD, as suggested by a recent review[38]. We also conducted further analyses implementing Fine-Gray subdistribution models to assess the role of competing risks[39, 40]. All analyses were conducted using the SAS 9.4 software package. The proportional hazards assumptions of the Cox models were verified via the SAS ASSESS with the PH option (the supremum test) function under the PHREG procedure (p>0.20).

Results

The demographic characteristics of the study sample at MIDUS I are presented in Table 1. The sample of 1,870 participants consisted of approximately equal numbers of males and females and was mostly white, middle-aged, married, and had at least some college education. Most participants had low job strain in both MIDUS I and MIDUS II (84%) and did not experience an increase in job strain from MIDUS I to MIDUS II (89%). There was a total of 29 CVD mortality cases in the sample, and the CVD mortality rate was 1.11 per 1,000 person-years.

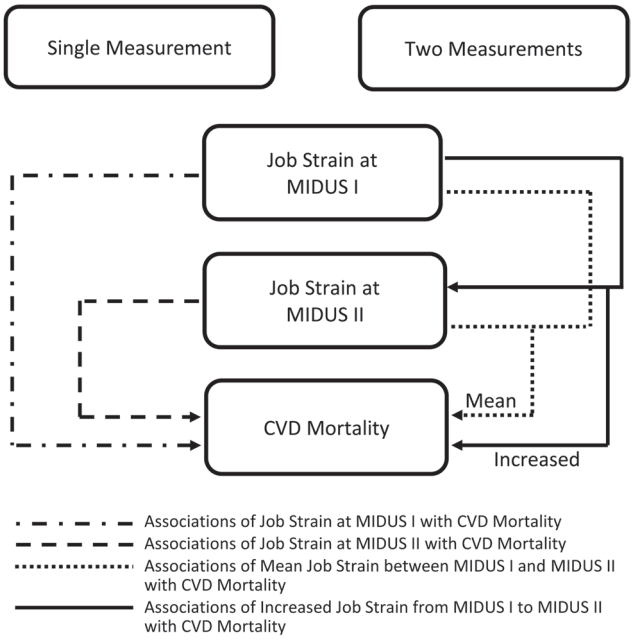

Fig. 2. Model of associations between job strain (MIDUS I and MIDUS II) with cardiovascular disease (CVD) mortality (N=1,870).

Table 2 shows the results of the Cox proportional hazards regression analyses. Though single job strain scores at MIDUS I and MIDUS II, and both mean and increase scores between the two waves were all not significantly associated with CVD mortality, increased job strain from MIDUS I to MIDUS II demonstrated stronger prospective associations with CVD mortality (HR and 95% CI=2.37 [0.88, 6.42]). As expected, additional adjustment for the health behaviors of smoking, alcohol consumption, and physical exercise at MIDUS II attenuated the association of increased job strain from MIDUS I to MIDUS II with CVD mortality (see Supplementary Table 6).

Discussion

In this national, population-based study of U.S. workers, increased job strain across two time points ten years apart exhibited stronger prospective associations with CVD mortality. Consistent with our hypotheses, increased job strain across two time points seemed to have larger predictive power in assessing associations of job strain with CVD mortality, compared with single measures of job strain at two time points or mean job strain across two time points. These results suggest that increasing job strain exposure may have a role in the pathophysiology of CVD. These results are consistent with previous studies on job strain CVD[5–12], especially recent work adopting a similar

Table 1. Characteristics of the study sample at MIDUS I (1995/1996) (*N*=1,870)

Variables		(*N*, %)
Sex		
Male		933 (49.89)
Female		937 (50.11)
Age (yr)		
<46		1,157 (61.87)
46–55		514 (27.49)
56+		199 (10.64)
Race		
White		1,759 (94.06)
Non-white:	Black and/or African American	58 (3.10)
	Native American or Aleutian Island/Eskimo	10 (0.53)
	Asian or Pacific Islander	9 (0.48)
	Other	21 (1.12)
	Multiracial	13 (0.70)
Marital status		
Married		1,323 (70.75)
Never married		245 (13.10)
Divorced/widowed/separated		302 (16.15)
Educational attainment		
University or more		812 (43.42)
Some college		557 (29.79)
High school or less		501 (26.79)
Household income (annual U.S. dollars)		
<60,000		541 (28.93)
60,000–99,999		541 (28.93)
≥100,000		788 (42.14)
MIDUS I job strain		
Low		1,562 (83.53)
High		308 (16.47)
MIDUS II job strain*		
Low		1,563 (83.58)
High		307 (16.42)
Mean job strain*		
Low		1,509 (80.70)
High		361 (19.30)
Increased job strain*		
No		1,673 (89.47)
Yes		197 (10.53)

*Data were based on information at MIDUS II (2004/2006) as well.

approach of using multiple measures of persistent and changing job strain[14].

While it is important to acknowledge that CVD risk is multifactorial and that there may be other contributing influences, the notion that job strain constitutes a clinically relevant risk factor for CVD is biologically plausible and mechanistically sound. The persistence or exacerbation of exposure to psychosocial stressors such as job strain may lead to dysfunction of the HPA axis, the initiation and progression of inflammatory processes such as atherosclerosis, and chronic overactivation of the sympathetic nervous system; such psychophysiological pathways are hypothesized to be the mechanisms underlying observed associations of job strain with CVD[41]. Additional potential mechanisms include high blood pressure—a recent study of 63,800 employees in the Netherlands identified

Table 2. Prospective associations of job strain with cardiovascular disease (CVD) mortality in the MIDUS Cohort (1995/1996–2018) (*N*=1,870, number of CVD deaths=29) (HRs and 95% CIs)

	Number of exposed participants (number of CVD deaths)	Model I	Model II
MIDUS I job strain			
Low	1,562 (24)	1.00	1.00
High	308 (5)	1.37 (0.51, 3.65)	1.29 (0.48, 3.49)
MIDUS II job strain			
Low	1,563 (27)	1.00	1.00
High	307 (2)	0.57 (0.13, 2.46)	0.54 (0.12, 2.32)
Mean strain			
Low	1,509 (25)	1.00	1.00
High	361 (4)	1.03 (0.35, 3.06)	1.02 (0.34, 3.06)
Increased strain			
No increase	1,673 (24)	1.00	1.00
Increase	197 (5)	2.53 (0.95, 6.76)	2.37 (0.88, 6.42)

CI: confidence interval; HR: hazards ratio.

Cox proportional hazards regression.

Model I: adjustment for age and sex at MIDUS I; Model II: Model I + additional adjustment for race, marital status, educational attainment, and household income at MIDUS I.

significant associations of higher job strain with higher systolic and diastolic blood pressure[42].

The lack of significant associations observed with single measures of job strain at two time points (baseline and 10 yr follow-up) and mean job strain across two time points imply an effect of potential exposure misclassification bias, where job strain exposures are not adequately assessed and parameterized, possibly leading to conservative effect estimates and overall downward bias. In longitudinal studies, changes in job strain exposure over time may have considerable implications for health outcomes; exposure models that include such changes are able to achieve a more comprehensive and nuanced mode of exposure assessment. In accordance with ongoing developments within the field of observational epidemiology, where inferences may be augmented by triangulation, or the combination of methodological approaches[14, 22, 24], our results emphasize the importance of sensitive measurements in overcoming exposure misclassification bias. This study adds to the weight of evidence supporting the deliberate use of multiple methodologies in assessing epidemiological health outcomes.

Our results may also be tempered by selection bias, predominantly the healthy worker survivor effect (HWSE), which broadly impacts studies of working populations and can be quite pronounced in studies of severe disease outcomes such as CVD mortality[43]. In our study, those individuals who were working in MIDUS I and still working in MIDUS II maintained their health status such that they were able to continue working; conversely, individuals with health complications or higher job strain at MIDUS I may have temporarily stopped working, permanently exited the labor market, or even passed away by MIDUS II, thereby excluding them from the analyses. Our primary objective was to assess changes in job strain, and thus only those who were working in both MIDUS I and MIDUS II were included into data analyses. Hence, the strength of association between job strain and CVD mortality might be underestimated due to the HWSE. Other biases that may impact our results include immortal time survival bias. Workers who survived and therefore could be included in the analyses may have differed from those who did not survive up to the beginning of the study[37]. Therefore, recourse of age as time scale and delayed entry age at beginning of the study were applied in all Cox regression analyses, in order to minimize immortal time survival bias. In a similar vein, we must consider the potential impact of differential occupational exposures across the study period. Workers with high exposures to job strain or at high risk for CVD may be more likely to undergo changes in exposure, ultimately leading to a possible bias in our results. While self-report measures of job strain may be susceptible to recall and reporting bias, questionnaire-based measures have been shown to be reliable and valid[44].

The fact that the supplementary analyses including additional adjustment for the health behaviors of smoking,

alcohol consumption, and physical exercise attenuated associations of increased job strain from MIDUS I to MIDUS II with CVD mortality suggests that these lifestyle factors have a mediating role. This is consistent with recent findings in the investigation of CVD in occupational epidemiology, wherein a growing body of literature has suggested that such health behaviors should not be included in statistical models as covariates, but treated as potential mediators of the relationship between job strain and CVD[38, 45]. As evidenced by our supplementary analyses, adjusting for such mediating factors would lead to conservative effect estimates. Furthermore, we conducted a series of sensitivity analyses to examine the robust associations of job strain with CVD mortality, including different operationalizations of job strain (such as quadrant method and traditional change categories), age as continuous variable, sex-specific analyses, and subdistribution and cause-specific hazard models for competing risk (see Supplementary Tables 2–11). Consistently, a pattern of stable associations between increased job strain and CVD mortality is suggested.

Strengths

The major strengths of this study are founded on the quality of the data and the methodological design. The MIDUS sample includes American workers across a broad range of demographic, professional, and clinical characteristics. Furthermore, the exposure measure of job strain was based on a well-established scale, and the health outcome of CVD mortality was based on empirical data from the NDI, increasing confidence in the accuracy and robustness of outcome assessment. This study is also methodologically unique as it utilizes multiple differing operationalizations of job strain across time points, reducing potential exposure misclassification bias and increasing the sensitivity of the analyses, thus overcoming limitations identified in previous studies. To the best of our knowledge, this is the first study examining the association between increased job strain and CVD mortality in a U.S. population.

Limitations

This study has several limitations. Most importantly, we observed substantial attrition rates from MIDUS I to MIDUS II among employed study subjects. Hence, our results may be impacted by selection bias; workers who were lost during follow up or who had stopped working in MIDUS II may have differed systematically from those retained in the sample. While the survey sample included members of racial and ethnic minority groups, the numbers of these individuals were too low to be grouped into their own racial categories, limiting the generalizability of our findings. Additionally, the number of fatal CVD events in the sample was relatively small (29). The number of fatal CVD events may have been lower due to the relatively young age of the sample, their status as members of the working population, and the limited follow-up period of the study. As a result, we were not able to conduct detailed analyses on CVD sub-groups, such as ischemic heart disease and stroke, respectively. Furthermore, this study did not address sub-clinical determinants of CVD such as hypertension and diabetes mellitus, which may have a mediating role in associations of job strain with CVD[46].

Conclusions

In a national, population-based sample of U.S. workers, increased job strain across ten years showed stronger prospective associations with CVD mortality compared to single measures of job strain at two time points and mean job strain across two time points. These results suggest that the intentional adoption of different methods of exposure assessment may be a critical factor in detecting potentially detrimental associations. The results of this study implicate increases in job strain exposure over time as a relevant risk factor for CVD mortality, emphasizing a role of psychosocial work exposures as novel and non-traditional drivers of cardiometabolic health. Healthcare initiatives administered by governments and employers, as well as workplace intervention programs, may benefit from the reduction of job strain as a critical risk to cardiovascular health.

Availability of Data and Material

All data analyzed during this study are included in this published article and also in the supplementary materials.

Authors' Contributions

JL conceived the research question and study design. TAM prepared the data. TAM and JL conducted the statistical analyses and wrote the draft of the manuscript. LC contributed to the line of argumentation and revision of the manuscript. All authors approved the final manuscript.

Conflict of Interest

The authors of this manuscript declare that they have no conflicting interests.

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