The Risk of Developing Diabetes in Association With Long Working Hours Differs by Shift Work Schedules

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ABSTRACT

Background: The impact of long working hours on diabetes is controversial; however, shift work is known to increase the risk of diabetes. This study aimed to investigate the association between long working hours and diabetes among civil servants in Japan separately by shift work schedules.

Methods: A prospective cohort study was conducted from April 2003 to March 2009. A total of 3195 men aged ≥35 years who underwent an annual health checkup at baseline were analyzed by shift work schedules (2371 non-shift workers and 824 shift workers). Self-reported working hours were categorized as 35–44 and ≥45 hours per week. The incidence of diabetes was confirmed by fasting plasma glucose concentration ≥126 mg/dL and/or self-reported medical diagnosis of diabetes at the annual checkup. A Cox proportional model was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing diabetes associated with long working hours.

Results: The median follow-up period of non-shift and shift workers was 5.0 and 4.9 years, respectively. During this period, 138 non-shift workers and 46 shift workers developed diabetes. A decreased HR was found among non-shift workers working ≥45 hours per week (HR 0.84; 95% CI, 0.57–1.24); however, shift workers working ≥45 hours per week had a significantly increased risk of diabetes (HR 2.43; 95% CI, 1.21–5.10) compared with those working 35–44 hours per week. An analysis restricted to non-clerical workers also showed similar results.

Conclusions: The risk of diabetes associated with long working hours differed by shift work schedules.

Key words: cohort study; occupational health; sex; shift work; working hours

INTRODUCTION

Long working hours is an important public health concern because of possible harmful effects on human health. A previous systematic review concluded that long working hours is associated with increased risks of coronary heart diseases, anxiety, depressive state, and detrimental sleep conditions.1 Regarding working hours, the average annual hours actually worked per worker in Organisation for Economic Co-operation and Development (OECD) countries decreased gradually from 1843 hours in 2000 to 1770 hours in 2013; a similar trend was observed in Japan, where annual hours per worker decreased from 1821 hours in 2000 to 1734 hours in 2013.2 However, it was estimated that 22.0% of workers worldwide worked more than 48 hours per week in 2007.3 In Japan, the proportion of workers working ≥49 hours per week was 22.9% in 2009 and 21.7% in 2013.4 Moreover, that proportion among civil servants in Japan increased from 17.4% in 2000 to 34.2% in 2010.5 Thus, it should be recognized that certain workers continue to work long hours.

Diabetes is a common and increasingly prevalent disease worldwide. The global prevalence of diabetes was estimated at 8.3% among adults in 2013, and it was predicted to increase to 10.1% in 2035.6 Complications of diabetes (eg, cardiovascular disease, nephropathy, nerve damage, and retinopathy) are major causes of disability, reduced quality of life, and death.6 Several studies have investigated the association between long working hours and diabetes7–10; however, the results were limited and inconsistent. From the results of three cohort studies,7–9 Kawakami et al indicated that long working hours significantly increased the risk of diabetes among Japanese male industrial workers.7 In contrast, one other study found a significantly decreased risk of diabetes in male office workers working long hours in Japan.8 Furthermore, no association was
found between working long hours and diabetes among female nurses in the United States. Finally, a cross-sectional study in Japan that included both sexes showed significantly decreased risks of diabetes associated with long working hours, except for workers with ≥100 hours of overtime per month.  

Referring to a previous report, possible reasons for this inconsistency might include differences in the study design, participant characteristics, categorization of working hours, the definition of diabetes, and the approach to shift work schedules (eg, analyzing separately by shift work schedules or adjusting those as covariates in statistical analysis).

In this study, we focused on the latter factor, because a previous review argued that it is important to deal properly with shift work schedules for clear interpretation, and a recent meta-analysis concluded that shift work is associated with an increased risk of diabetes. Based on these facts, we considered that statistical analyses needed to be conducted separately by shift work schedules when investigating the association between long working hours and diabetes. However, no prospective cohort study to date has followed this approach. The purpose of this study was to prospectively explore the association between long working hours and diabetes separately by shift work schedules among civil servants in Japan.

**METHODS**

**Study design and participants**

This was a prospective cohort study conducted from April 2003 to March 2009 in Sapporo City, Hokkaido Prefecture, Japan. The study population consisted of civil servants aged ≥35 years (total \( n = 10,423 \); 8229 men and 2194 women) who underwent an annual health checkup between April 2003 and March 2004. Self-administered questionnaires were distributed to them before their health checkup. Those agreeing to participate in this study provided written informed consent and completed the questionnaires, which were then collected during the checkup.

A total of 3962 men and 1051 women consented to participate in this study at baseline (response rate: 48.1% for men and 47.9% for women). Because few women developed diabetes during the study period (\( n = 28 \)), only men were analyzed in this study. For follow-up of at least 1 year, we excluded 176 men aged ≥59 years who would reach retirement within that period. We also excluded 199 men with fasting plasma glucose (FPG) concentration ≥126 mg/dL, and/or who self-reported a diagnosis of diabetes by a medical doctor. In this study, participants with medical histories of angina pectoris (\( n = 25 \)), acute myocardial infarction (\( n = 16 \)), and brain stroke or hemorrhage (\( n = 29 \)) were also excluded.

Working hours were self-reported as hours worked per week. In this study, we considered that participants who worked at least ≥35 hours per week were eligible because their contracted working time was 38.75 hours per week. A total of 88 participants who did not meet this criterion were excluded.

Three participants who stated that they worked extremely long working hours (eg, 490 hours per week) were excluded because their responses were considered erroneous. Thirty three participants with missing data for working hours or shift work schedules were also excluded. After the first checkup, 198 men did not undergo the subsequent checkup during the study period. Therefore, the total study sample for analysis comprised 3195 men. The study protocol was approved by the Ethics Committee of Hokkaido University Graduate School of Medicine.

**Working hours, shift work schedules, and diabetes**

In the questionnaire, participants were asked about their working hours at baseline using the following question: “During the last month, excluding summer vacations or a week containing many holidays, how many hours on average in a week did you work, including unpaid overtime work?” Participants reported their working hours as a continuous variable, and working hours were then categorized as 35–44 or ≥45 hours per week. We defined long working hours as ≥45 hours per week. Because the number of working hours may be affected by seasonal variations, we added the month in which participants underwent their annual health checkup at baseline as a covariate. Shift work schedules were also queried in the questionnaire (no shift work, or shift work with or without night shifts). Because there were few cases of shift work with no night shifts (\( n = 48 \)), shift work schedules were categorized as non-shift work or shift work.

The incidence of diabetes was confirmed by FPG concentration ≥126 mg/dL and/or self-reported diagnosis of diabetes by a medical doctor based on the questionnaire completed at the annual health checkup after the baseline. FPG concentration was measured from a blood sample drawn from the antecubital vein of the seated participant, with minimal tourniquet use after a 12-hour fast, using the amperometric method (Arkray, Kyoto, Japan). We did not ask participants about the type of diabetes because they may have not remembered this information correctly. In Japan, type 2 diabetes is common, but the incidence of type 1 diabetes among adults is very low. The date of diabetes onset was defined as having or having had a first-degree relative with diabetes.

**Other data collection**

Basic characteristics of participants were gathered, such as age, educational level (≤12 years or ≥12 years), marital status (married, others, or unknown), and job category (clerical workers, professional workers, manual workers, or fire fighters). For example, professional workers included
doctors, nurses, pharmacists, physiotherapists, radiographers, and technicians. Manual workers included conductors, drivers, garbage workers, machine operators, mechanics, and school janitors. Body mass index (BMI) was calculated from data obtained at the baseline health checkup. Lifestyle habits were assessed, including smoking status (current smoker or not), drinking habits (every day, sometimes, or never), and exercise habits (≥2 times per week and ≥30 minutes per session14; yes, others, or unknown). Hypertension (yes or no) was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or self-reported treatment for hypertension at baseline. Blood pressure was measured using an automated sphygmomanometer (USM-700G Si; Ueda Avancer Corp., Tokyo, Japan) placed on the arm of a seated participant who had been seated for a few minutes before measurement.

Statistical analysis
First, we showed descriptive statistics about the basic characteristics of the participants according to working hours by shift work schedules. Second, multivariate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing diabetes associated with long working hours were calculated separately by shift work schedules using a Cox proportional model. Participants working 35–44 hours per week were used as the reference category. We constructed three models: model 1 was adjusted for basic information of diabetes, such as age, FPG concentration at baseline, family history of diabetes, and the month in which participants underwent their annual health checkup at baseline; model 2 was additionally adjusted for basic characteristics of participants, such as educational level, marital status, and job category; model 3 was additionally adjusted for BMI, smoking status, drinking habits, exercise habits, and hypertension at baseline. We then treated working hours as continuous variables and calculated HRs for the association between increasing working hours by 10 hours per week and developing diabetes. Finally, to assess potential effect modification by shift work, we further analyzed the interaction model, including working hours as categorical variables, shift work schedules, the multiplicative interaction term, and the same covariates as in model 3.

Two-tailed tests were used, and P-values below 0.05 were considered statistically significant. All statistical analyses were performed using JMP Pro 11.0.0 for Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS
The median follow-up period was 5.0 years for non-shift workers (n = 2371) and 4.9 years for shift workers (n = 824). During this period, 138 non-shift workers and 46 shift workers developed diabetes. The incidence of diabetes was 13.4 per 1000 person-years for non-shift workers and 12.6 per 1000 person-years for shift workers.

Table 1 shows the characteristics of non-shift and shift workers by working hours. Compared with those working 35–44 hours per week, both non-shift and shift workers working ≥45 hours per week were more likely to be young and firefighters and to have low FPG concentration at baseline and were less likely to be manual workers and to have daily or no drinking habits. In addition to these, non-shift workers working ≥45 hours per week were more likely to have high educational level and to be professional workers and were less likely to be current smokers and to have exercise habits and hypertension. Shift workers working ≥45 hours per week were more likely to be current smokers and were less likely to be professional workers.

HRs for the incidence of diabetes associated with long working hours by shift work schedules are shown in Table 2. Non-shift workers working ≥45 hours per week had decreased HRs compared with those working 35–44 hours per week in all models, but these were not significant. HRs for each 10-hour increase in working hours per week were also decreased, and significant HRs were found in models 2 and 3 (HR 0.71; 95% CI, 0.49–0.99 for both models). On the other hand, shift workers working ≥45 hours per week had a significantly increased risk of diabetes compared with those working 35–44 hours per week in all models (HR 2.36; 95% CI, 1.22–4.79, HR 2.26; 95% CI, 1.17–4.57, and HR 2.43; 95% CI, 1.21–5.10 in models 1–3, respectively). HRs for each 10-hour increase in working hours per week were not significant among shift workers; however, HRs were greater than 1.0. Effect modification by shift work was significant (P for interaction = 0.02).

Additionally, we carried out an analysis of non-clerical workers only (n = 2124) by shift work schedules, as shown in Table 3. We did this because the majority of shift workers were non-clerical workers. The results were relatively similar to those found in the analysis of all participants. In model 3, the HR for workers working ≥45 hours per week was 0.90 (95% CI, 0.52–1.52) among non-shift workers and 2.28 (95% CI, 1.13–4.82) among shift workers, compared with those working 35–44 hours per week.

Based on the significant results among shift workers, we further divided the categories of long working hours into 45–54 (17 cases per 1417 person-years) and ≥55 (12 cases per 828 person-years) hours per week and then explored the association between long working hours and diabetes in the same way as in model 3. HRs were 2.55 (95% CI, 1.16–5.75) for shift workers working 45–54 hours per week and 2.26 (95% CI, 0.92–5.50) for those working ≥55 hours per week, compared with those working 35–44 hours per week.

DISCUSSION
This is the first prospective cohort study to investigate the association between long working hours and diabetes separately by shift work schedules.
Table 1. Baseline characteristics of male participants according to shift work schedules and working hours (n = 3195)

| Working hours | Non-shift workers (n = 2371) | Shift workers (n = 824) |
|---------------|-----------------------------|-------------------------|
|               | (n = 1435)                  | (n = 936)               |
|               | (n = 327)                   | (n = 497)               |
| Mean (SD) age | 49.1 (6.3)                  | 46.1 (6.4)              |
| Mean (SD) FPG, mg/dL | 92.9 (10.0)               | 91.7 (9.2)              |
| Family history of diabetes |                     |                         |
| Yes | 205 (14.3) | 130 (13.9) | 46 (14.1) | 74 (14.9) |
| Educational level |                        |                         |
| >12 years | 734 (51.1) | 524 (56.0) | 51 (15.6) | 91 (18.3) |
| Marital statusa |                   |                         |
| Married | 1232 (85.8) | 819 (87.5) | 301 (92.0) | 442 (88.9) |
| Others | 202 (14.1) | 117 (12.5) | 26 (8.0) | 55 (11.1) |
| Job category |                     |                         |
| Clerical | 622 (43.3) | 402 (42.9) | 13 (4.0) | 34 (6.9) |
| Professional | 474 (33.0) | 373 (39.9) | 43 (13.2) | 37 (7.4) |
| Manual | 312 (21.8) | 75 (8.0) | 160 (48.9) | 176 (35.4) |
| Fire fighters | 27 (1.9) | 86 (9.2) | 111 (33.9) | 250 (50.3) |
| Mean (SD) BMI, kg/m² | 23.7 (2.8) | 23.8 (2.7) | 24.1 (3.1) | 24.1 (3.0) |
| Smoking status |                     |                         |
| Current | 684 (47.7) | 407 (43.5) | 165 (50.5) | 300 (60.4) |
| Drinking habits |                   |                         |
| Every day | 638 (44.5) | 398 (42.5) | 100 (30.6) | 112 (22.5) |
| Sometimes | 564 (39.3) | 422 (45.1) | 169 (51.7) | 317 (63.8) |
| Never | 233 (16.2) | 116 (12.4) | 58 (17.7) | 68 (13.7) |
| Exercise habitsb,c |                 |                         |
| Yes | 337 (23.5) | 180 (19.2) | 127 (38.8) | 188 (37.8) |
| Others | 1087 (75.7) | 750 (80.1) | 198 (60.6) | 305 (61.4) |
| Hypertensiond |                   |                         |
| Yes | 208 (14.5) | 106 (11.3) | 46 (14.1) | 67 (13.5) |

BMI, body mass index; FPG, fasting plasma glucose; SD, standard deviation.  
aFPG concentration at baseline.  
bTotal proportion does not add to 100% owing to missing data.  
cExercise habits refer to ≥2 times per week and ≥30 minutes per session.  
dHypertension is defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or under treatment at baseline.

Table 2. Hazard ratios for the incidence of diabetes associated with long working hours by shift work schedules among all participants (non-shift workers n = 2371, shift workers n = 824)

| Working Hours | Person-years | Case | Model 1a | Model 2b | Model 3c |
|---------------|--------------|------|----------|----------|----------|
| Non-shift workers | 6022 | 93 | 1.00 (95% CI: 0.84–1.18) | 1.00 (95% CI: 0.84–1.18) | 1.00 (95% CI: 0.84–1.18) |
| ≥45 h/week | 4295 | 45 | 0.83 (0.67–1.02) | 0.79 (0.63–1.00) | 0.84 (0.68–1.03) |
| Per 10-hour increase | 0.74 (0.52–1.02) | 0.70 (0.49–1.00) | 0.71 (0.49–1.00) |
| Shift workers | 6022 | 93 | 1.00 (95% CI: 0.84–1.18) | 1.00 (95% CI: 0.84–1.18) | 1.00 (95% CI: 0.84–1.18) |
| ≥45 h/week | 4295 | 45 | 0.83 (0.67–1.02) | 0.79 (0.63–1.00) | 0.84 (0.68–1.03) |
| Per 10-hour increase | 0.74 (0.52–1.02) | 0.70 (0.49–1.00) | 0.71 (0.49–1.00) |

CI, confidence interval; HR, hazard ratio.  
aAdjusted for age, fasting plasma glucose concentration at baseline, family history of diabetes (yes, no), and month in which participants underwent their annual health checkup at baseline.  
bModel 1+ additionally adjusted for educational level (≤12 years, >12 years), marital status (married, others, unknown), and job category (clerical workers, professional workers, manual workers, fire fighters).  
cModel 2+ additionally adjusted for body mass index, smoking status (current smoker or not), drinking habits (every day, sometimes, never), exercise habits (≥2 times per week and ≥30 minutes per session) (yes, others, unknown), and hypertension at baseline (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or under treatment) (yes, no).  
dCase refers to diabetes.  
eHRs for the association between increasing working hours by 10 hours per week and developing diabetes.
In this study, non-shift workers tended to show decreased risks of diabetes associated with long working hours, even when the analysis was restricted to non-clerical workers. Previous studies also indicated a significantly decreased risk of diabetes among non-shift workers with long working hours. Nakanishi et al performed a prospective cohort study and showed that non-shift workers working ≥11.0 hours per day had a significantly decreased risk of diabetes compared with those working <8.0 hours per day (relative risk 0.30). Kuwahara et al conducted a cross-sectional study and found that non-shift workers working 45–79 or 80–99 hours of overtime per month had significantly decreased risks compared with those working <45 hours of overtime per month (odds ratios 0.86 and 0.59, respectively). These results suggest a possible decreased risk of diabetes among non-shift workers who work long hours; however, additional cohort studies with large sample sizes are needed.

The potential mechanisms involved in the protective effects of developing diabetes associated with long working hours among non-shift workers are not clear. However, as argued by Nakanishi et al, the differences in 24-hour energy expenditure among non-shift workers in accordance with the length of working hours observed in their study may be related to the results. They found that the longer non-shift workers worked, the more highly they exhibited energy expenditure. Although we did not evaluate energy expenditure in this study, this might be one of the potential explanations for such findings.

To our knowledge, this is the first study to document that shift workers with long working hours had a significantly increased risk of diabetes. A previous cross-sectional study showed no association between long working hours and diabetes among shift workers. However, as previously mentioned, differences in study design, sample size, categories of working hours, covariates, and results shown by sex or not are considered potential reasons for inconsistency with previous reports. Because the present study is a prospective cohort study, the temporality is clearer than in a previous cross-sectional study.

Potential explanations for developing diabetes among shift workers with long working hours can be inferred from previous studies. One of the important physiological problems associated with shift work schedules is that eating and sleeping phases are changed. Concerning eating, shift work schedules may lead to changes in daily eating patterns, such as irregular meal frequency and intake, especially among workers with long working hours. Both of these irregular eating patterns are considered to be associated with insulin resistance and may lead to the development of diabetes.

Regarding sleeping, Buxton et al indicated that prolonged sleep restriction with concurrent circadian disruptions, as may occur among shift workers, reduced the resting metabolic rate and caused a reduction in insulin secretion. Sleep restriction is reported to be significantly associated with increases in cortisol, interleukin-6, and tumor necrosis factor-α, and these changes may contribute to insulin resistance. Sleep deprivation is also associated with decreased leptin levels, increased ghrelin levels, and increased hunger and appetite. Moreover, the sympathetic nervous system may be activated by sleep deprivation, leading to increased blood pressure and heart rate, and hypertension is a known risk factor for diabetes. Additionally, long working hours aggravates sleep conditions, which may lead to the development of diabetes.

The third health risk is related to stress. Occupational stress, such as effort-reward imbalance (ERI), is pointed out to be more prevalent among shift workers than daytime workers, and long working hours is also associated with ERI. ERI is related to increased risk of diabetes. In addition to occupational stress, shift workers may experience more stress...
related to their family or social life than non-shift workers. Because shift work schedules can experience considerable disruption of family and social activities as many of these rhythms of the general population are oriented around the day, moreover, this situation may be worsened by long working hours. It is known that stress is associated with concurrent activation of the hypothalamic-pituitary-adrenal axis, which may contribute to insulin resistance through the effects of glucocorticoids.

In this study, we observed a relatively high incidence of diabetes among shift workers, compared with that reported in two former Japanese cohort studies among men. The total incidence of diabetes in our study was 13.2 per 1000 person-years (13.4 per 1000 person-years among non-shift workers). This was higher than that reported in Kawakami’s study, in which 46.3% of subjects were shift workers (1.95 per 1000 person-years) and in Nakanishi’s study, which included only non-shift workers (9.1 per 1000 person-years). These two previous studies were conducted in 1984–1992 and in 1994–1999, respectively, and our study was performed in 2003–2009. The secular trend of diabetes prevalence in Japan may be related to differences in the incidence of diabetes.

In addition, disparities in the definition of diabetes may have affected study results. Kawakami et al defined diabetes following the WHO criteria (1980). Participants were first screened for glucosuria at a routine health checkup, and then FPG concentration was measured in participants with glucosuria. Finally, participants with FPG concentration ≥110 mg/dL underwent a 75 g oral glucose tolerance test to determine the diagnosis of diabetes. Nakanishi et al defined diabetes following the American Diabetes Association 1997 criteria for epidemiological studies. The incidence of diabetes was confirmed by FPG concentration ≥126 mg/dL or use of hypoglycemic medication. Our definition of diabetes was similar to the latter, but instead of medication use, we used a diagnosis of diabetes by a medical doctor that was self-reported on our questionnaire, because some participants may have developed diabetes but chose not to undergo treatment. The definition of diabetes by Kawakami et al was stricter than that used here or by Nakanishi et al. Therefore, the incidence was comparatively low. In recent years, a recommendation to use HbA1c for diagnosis of diabetes was issued in a report by the International Expert Committee on diabetes. We did not use HbA1c for the diagnosis of diabetes in this study because only 26.0% of participants had HbA1c data at baseline. We consider that the definition of diabetes in epidemiological studies needs to be discussed and standardized for further studies.

There are several strengths in the present study. First, our study is a prospective cohort study design. The second strength is related to our approach for investigating the association between long working hours and incidence of diabetes. Following previous reports, we defined long working hours as ≥45 hours per week, conducted statistical analysis separately by shift work schedules, and defined the reference group as participants working 35–44 hours per week. Because of our clear definition of long working hours and exclusion of the influence of shift work, we believe these approaches contribute to clear interpretation of our results.

Nonetheless, our study has some limitations. First, the number of participants and the number of new onset of diabetes in our study were relatively small. This led to low statistical power, and there is a possibility that we could not find significant associations other than those obtained. Second, detailed information about shift work schedules, such as duration, types (eg, two-shift, three-shift), and frequency (eg, times per week) was not obtained. As a result, shift work schedules in this study may vary on these points, and small differences in shift work schedules among shift workers might affect the results. Third, data on working hours were self-reported and might, therefore, include some inaccuracies. This may lead to non-differential misclassification, and HRs may be attenuated toward 1.0. Nevertheless, this study found risks of diabetes associated with long working hours among shift workers. Fourth, the relatively low response rate in our study might lead to difficulty in generalizing the results. Information on non-responders could not be obtained, so we could not compare the characteristics of non-responders with those of responders. However, a total of 94.2% of the participants were followed up in our study, which strengthens our findings.

In conclusion, we prospectively investigated the association between long working hours and diabetes by shift work schedules among male civil servants in Japan. We found that long working hours increased the risk of incident diabetes among shift workers. Meanwhile, the results among non-shift workers suggest the possibility of decreased risk of diabetes associated with long working hours. It is important to take shift work schedules into consideration when implementing health care measures for the prevention of diabetes among male workers.

ONLINE ONLY MATERIAL

Abstract in Japanese.

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