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Original Article

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Effect of night shift work on the reduction of glomerular filtration rate using data from Korea Medical Institute (2016-2020)

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ABSTRACT

Background: Shift work increases the risk of chronic diseases, including metabolic diseases. However, studies on the relationship between shift work and renal function are limited. The aim of this study was to investigate the association between shift work and a decreased glomerular filtration rate (GFR).
Methods: Data were evaluated for 1,324,930 workers who visited the Korean Medical Institute from January 1, 2016 to December 31, 2020 and underwent a health checkup. Daytime workers were randomly extracted at a ratio of 1:4 after matching for age and sex. In total, 18,190 workers aged over 40 years were included in the analyses; these included 3,638 shift workers and 14,552 daytime workers. Participants were categorized into the shift work group when they underwent a specific health checkup for night shift work or indicated that they were shift workers in the questionnaire. The odds ratio was calculated using a conditional logistic regression to investigate the relevance of shift work for changes in GFR.
Results: 35 workers in the shift group and 54 in the daytime group exhibited an estimated GFR (eGFR) value of < 60 mL/min/1.73m^2 ($p < 0.01$). The difference in eGFR values between two checkups differed significantly depending on the type of work ($p < 0.01$); the difference in the shift work group (−9.64 mL/min/1.73 m^2) was larger than that in the daytime work group (−7.45 mL/min/1.73 m^2). The odds ratio for eGFR reduction to < 60 mL/min/1.73 m^2 in the shift group versus the daytime group was 4.07 (95% confidence interval: 2.54–6.52), which was statistically significant.
Conclusions: The results of this study suggest that eGFR decreases by a significantly larger value in shift workers than in daytime workers; thus, shift work could be a contributing factor for chronic kidney disease (CKD). Further prospective studies are necessary to validate this finding and identify measures to prevent CKD in shift workers.

Keywords: Chronic disease; Metabolic diseases; Glomerular filtration rate; Kidney failure, chronic

BACKGROUND

In 2020, 145,006 patients were undergoing renal replacement therapy (RRT; RRT include hemodialysis, peritoneal dialysis, and renal transplantation) in Korea, with 18,379 new

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Competing interests

The authors declare that they have no competing interests.

Author Contributions

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patients placed on RRT in 2019 alone. The major causes of chronic renal failure include diabetic nephropathy (49.8%), hypertensive glomerulosclerosis (20.5%), and chronic glomerulonephritis (8.5%).[1] In normal individuals, the glomerular filtration rate (GFR) declines at a rate of 0.8–1 mL/min/1.73 m^2 per year after 40 years of age. In the general population, a GFR decline rate of ≥ 3 mL/min/1.73 m^2 is considered rapid, whereas in individuals with chronic renal failure, a decline rate of ≥ 5 mL/min/1.73 m^2 per year is considered rapid.

Chronic kidney disease (CKD) is defined as the presence of kidney damage as evidenced by proteinuria or hematuria or an estimated GFR (eGFR) value of < 60 mL/min/1.73 m^2 that persists for ≥ 3 months.[2] The prevalence of CKD is consistently rising with the increasing prevalence of chronic diseases such as diabetes mellitus (DM) and hypertension (HTN) and an increase in the older adult population.[3] Diabetic nephropathy is mainly characterized by persistent albuminuria and diminished renal function. HTN is a major cause of renal disease. Atherosclerotic HTN-related diseases primarily affect the renal arterioles before affecting the glomerulus, leading to ischemic changes in the glomerulus and post-glomerular structures. Consequently, renal injury progresses and nephrons are lost, resulting in a vicious cycle of more severe HTN, glomerular hyperfiltration, and renal damage.

According to the fifth Korean Work Conditions Survey (KWCS), 9.7% of all workers performed shift work in 2017; this proportion had steadily increased from 7.2% in 2006. Although the actual number of individuals working in shifts differs across reports, approximately 1.2–2 million people are estimated to be shift workers. A 2017 report from the Ministry of Labor showed that 34.2% shift workers worked 12-hour shifts in two teams, while 27.5% worked every other day in two teams. In general, shift work disrupts the endogenous circadian rhythm and adversely affect biological homeostasis.[4] It has also been reported as a risk factor for cardiovascular disease[5] and metabolic disorders.[6]

Shift work also impairs kidney function. Previous studies have reported that police officers working night shifts have poorer kidney function than do those working day shifts,[7] and that sleep-deprived civil servants working in shifts are at increased risk for CKD.[8] Most previous studies on shift work investigated its relationship with cardiovascular diseases, and studies on the relationship between shift work and CKD have been limited to certain occupations. Therefore, the aim of this study was to investigate the effects of shift work on GFR.

METHODS

Participants

Data were evaluated for 1,324,930 workers who underwent a health checkup at the Korea Medical Institute (KMI) between January 1, 2016 and December 31, 2020. In general, for normal individuals, the GFR is known to decline by approximately 0.8–1 ml/min/1.73 m^2 per year after the age of 40 due to aging. Additionally, due to the low number of shift workers among individuals aged 60 and above, they were excluded from the study population. As a result, the final study population included individuals who were 40 years or older but less than 60 years at the start of the survey and had undergone at least two rounds of health checkups. The exclusion criteria were as follows: a diagnosis of cancer, HTN, DM, hyperlipidemia, or CKD at time of the study; a blood creatinine level of < 0.5 mg/dL; an eGFR value of < 60 mL/min/1.73 m^2; a and a change in the type of work (change from a rotating shift to a daytime schedule or vice versa). A total of 145,460 workers, including 3,638 shift workers

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and 141,822 daytime workers, were identified. Participants were randomly extracted at a ratio of 1:4 after matching for age and sex using the RAND function of Excel 2019 software.[9] In total, 3,638 shift workers and 14,552 daytime workers were eventually selected.

Variables

Shift workers were defined as those who underwent a specific health checkup for night shift work or were marked as "shift worker" in the questionnaire. Other workers were classified as daytime workers. The participants' age was categorized as 40–49 years and 50–59 years. eGFR was calculated using the eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Obesity was determined using the body mass index (BMI), which was categorized as < 23 kg/m^2, 23–24.9 kg/m^2, and ≥ 25 kg/m^2 according to the Asia-Pacific criteria.[10] Blood pressure was measured using an automatic blood pressure monitor. The participants were asked to sit for at least 5 minutes, and blood pressure readings were taken from the brachial artery. Hypertension is defined as a condition in which the systolic blood pressure was ≥140mmHg, and/or the diastolic blood pressure was ≥ 90 mmHg. On the basis of their smoking history, participants were categorized as nonsmokers (< 100 cigarettes smoked in their lifetime), current smokers, and ex-smokers. On the basis of their alcohol consumption habits, participants were categorized as nondrinkers, moderate drinkers (≤ 8 drinks/week for men, ≤ 4 drinks/week for women), and heavy drinkers (> 8 drinks/week for men, > 4 drinks/week for women).

Because all enrolled participants underwent at least two rounds of health checkups, the date of the first checkup was defined as the start of the observation period and the date of the final checkup was defined as the end of the observation period. The examination period was based on the difference between the last checkup date and the first checkup date. The difference in eGFR between the end and start of the observation period was defined as the change in eGFR.

Statistical analysis

The mean values of continuous variables were analyzed using the *t*-test and analysis of variance (ANOVA), whereas the frequencies of categorical variables were analyzed using the chi-square test. Following conditional logistic regression analysis, to examine the association between shift work and changes in eGFR, odds ratios (ORs) were calculated using the multivariate conditional logistic regression model after adjusting for demographic and individual factors. The study data were analyzed using SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). A *p*-value of < 0.05 was considered statistically significant.

Ethics statement

The protocol of this study was reviewed and approved by the Institutional Review Board of Dankook University (approval No. DKU 2022-02-024). The need for informed consent was waived by the board.

RESULTS

General characteristics of the participants

A total of 2,807 (20.0%) men and 831 (20.0%) women worked in shifts. By age, the study population comprised 12,230 individuals aged 40–49 years (67.2%) and 5,960 individuals aged 50–59 years (32.8%); 2,446 (19.6%) and 1,192 (20.6%) workers in the former and latter age groups, respectively, were shift workers. The proportion of nondrinkers was 55.3% (n = 2,011) in the shift worker group and 46.1% (n = 6,710) in the daytime worker group. We analyzed the difference in examination periods between the shift workers and daytime workers using a *t*-test. The results showed that the mean examination period for the daytime work group was 934 days (standard deviation [SD]: 402.8), while the mean examination period for the shift work group was 936 days (SD: 402.3). The *p*-value was 0.71, indicating that there was no statistically significant difference between the 2 groups. The two groups showed no significant differences in the BMI, and smoking status. The above results is the result at the first examination (**Table 1**).

Number of participants with eGFR values of < 60 mL/min/1.73 m²

Thirty-five participants in the shift work group (1.0%) and 54 in the daytime work group (0.4%) had an eGFR value of < 60 mL/min/1.73 m^2; these included 40 women (1.0%) and 49 men (0.3%). With respect to age, 25 participants aged 40–49 years (0.3%) and 64 participants aged 50–59 years (0.7%) had an eGFR value of < 60 mL/min/1.73 m^2. By smoking status, 55 (0.7%) nonsmokers, 7 (0.4%) current smokers, and 27 (0.3%) ex-smokers had an eGFR value of < 60 mL/min/1.73 m^2. By alcohol consumption status, 27 (0.6%) nondrinkers, 55 (0.5%) moderate drinkers, and 7 (0.2%) heavy drinkers had an eGFR value of < 60 mL/min/1.73 m^2. Fifty-one (5.6%) participants diagnosed with DM at time of end of observation and 38 (0.2%) without a diagnosis of DM had an eGFR value of < 60 mL/min/1.73 m^2. For each category, differences in the number of participants with an eGFR value of < 60 mL/min/1.73 m^2 were statistically significant ($p < 0.01$). However, no significant differences were observed in the groups based on obesity, and HTN diagnosis at the end of the observation period (**Table 2**).

Average eGFR change according to the general characteristics of the participants

Changes in eGFR significantly varied according to the type of work (shift work group: −9.64 mL/min/1.73 m^2 vs. daytime work group: −7.45 mL/min/1.73 m^2, $p < 0.01$), sex (men: −8.40 mL/min/1.73 m^2 vs. women: −5.81 mL/min/1.73 m^2, $p < 0.01$), age (40–49-year group: −8.12 mL/min/1.73 m^2 vs. 50–59-year group: −7.68 mL/min/1.73 m^2, $p < 0.01$), obesity (23–24.9 kg/m^2

Table 1. General characteristics of the participants

Characteristics	Work shift			*p*-value
	Daytime work	Shift work	Total	
Total	14,552	3,638	18,190	
Sex				0.51
Female	3,324 (22.8)	831 (22.8)	4,155 (22.8)	
Male	11,228 (77.2)	2,807 (77.2)	14,035 (77.2)	
Age (years)				0.04
40–49	9,784 (67.2)	2,446 (67.2)	12,230 (67.2)	
50–59	4,768 (32.8)	1,192 (32.8)	5,960 (32.8)	
BMI (kg/m^2)				0.77
< 23	5,347 (36.7)	1,341 (36.9)	6,688 (36.8)	
23–24.9	4,148 (28.5)	1,054 (29.0)	5,202 (28.6)	
≥ 25	5,057 (34.8)	1,243 (34.2)	6,300 (34.6)	
Smoking				0.07
Nonsmoker	5,901 (40.6)	1,447 (39.8)	7,348 (40.4)	
Ex-smoker	4,108 (28.2)	985 (27.1)	5,093 (28.0)	
Current smoker	4,543 (31.2)	1,206 (33.2)	5,749 (31.6)	
Alcohol consumption				< 0.01
Nondrinker	6,710 (46.1)	2,011 (55.3)	8,721 (47.9)	
Moderate drinker	4,045 (27.8)	886 (24.4)	4,931 (27.1)	
Heavy drinker	3,797 (26.1)	741 (20.4)	4,538 (24.9)	

Values are presented as number (column percent, %).
BMI: body mass index

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Table 2. Number of participants with eGFR values of < 60 mL/min/1.73 m^2

Variables	eGFR < 60 mL/min/1.73 m^2			p-value
	No	Yes	Total No.	
Work shift				< 0.01
Daytime work	14,498 (99.6)	54 (0.4)	14,552	
Shift work	3,603 (99.0)	35 (1.0)	3,638	
Sex				< 0.01
Female	4,115 (99.0)	40 (1.0)	4,155	
Male	13,986 (99.7)	49 (0.3)	14,035	
Age (years)				< 0.01
40–49	8,770 (99.7)	25 (0.3)	8,795	
50–59	9,331 (99.3)	64 (0.7)	9,395	
BMI (kg/m^2)				
< 23	6,174 (99.3)	20 (0.3)	6,194	
23–24.9	5,229 (99.5)	27 (0.5)	5,256	
≥ 25	6,698 (99.4)	42 (0.6)	6,740	
Smoking				< 0.01
Non-smoker	7,565 (99.3)	55 (0.7)	7,620	
Ex-smoker	8,916 (99.7)	27 (0.3)	8,943	
Current smoker	1,620 (99.6)	7 (0.4)	1,627	
Drinking				0.02
Non-drinker	4,175 (99.4)	27 (0.6)	4,202	
Moderate drinker	10,583 (99.5)	55 (0.5)	10,638	
Heavy drinker	3,343 (99.8)	7 (0.2)	3,350	
DM				< 0.01
No	17,249 (99.8)	38 (0.2)	17,287	
Yes	852 (94.4)	51 (5.6)	903	
HTN				0.84
No	17,852 (99.5)	88 (0.5)	17,940	
Yes	249 (99.6)	1 (0.4)	250	

Values are presented as number (row percent, %).
eGFR: estimated glomerular filtration rate; BMI: body mass index; DM: diabetes mellitus; HTN: hypertension.

group: −8.08 mL/min/1.73 m^2 vs. < 23 kg/m^2 group: −7.19 mL/min/1.73 m^2 and ≥ 25 kg/m^2 group: −8.38 mL/min/1.73 m^2, $p < 0.01$), smoking status (current smokers: −9.56 mL/min/1.73 m^2 vs. nonsmokers: −7.02 mL/min/1.73 m^2 and ex-smokers: −8.32 mL/min/1.73 m^2, $p < 0.01$), drinking status (heavy drinkers: −7.82 mL/min/1.73 m^2 vs. nondrinkers: −6.78 mL/min/1.73 m^2 and moderate drinkers: −8.34 mL/min/1.73 m^2), DM (no: −6.87 mL/min/1.73 m^2 vs. yes: −27.37 mL/min/1.73 m^2), and HTN (no: −7.84 mL/min/1.73 m^2 vs. yes: −10.79 mL/min/1.73 m^2, $p < 0.01$; **Table 3**).

Adjusted OR for the effect of shift work on eGFR reduction

Table 4 shows the results of conditional logistic regression modeling performed to examine the effects of shift work on eGFR. Compared with daytime workers, shift workers had significantly higher odds for an eGFR decrease to < 60 mL/min/1.73 m^2, with OR of 2.61 (95% confidence interval [CI]: 1.63–4.18). The odds for a decrease in eGFR to < 60 mL/min/1.73 m^2 remained higher (OR: 1.52; 95% CI: 2.54–6.52) for shift workers than for daytime workers after adjustment for demographic and individual factors.

DISCUSSION

In the present study, shift workers, compared with daytime workers, showed significantly higher odds for a decrease in eGFR to < 60 mL/min/1.73 m^2. Zhang et al.[11] examined the correlation between the duration of shift work and diminished eGFR in steel workers aged

Table 3. Average eGFR difference according to the general characteristics of the participants

Variables	eGFR difference	*p*-value
Work shift		< 0.01
Daytime work	−7.45 ± 13.22	
Shift work	−9.64 ± 12.52	
Sex		< 0.01
Female	−5.81 ± 15.31	
Male	−8.40 ± 12.32	
Age (years)		0.02
40–49	−8.12 ± 13.36	
50–59	−7.68 ± 12.86	
BMI (kg/m²)		< 0.01
< 23	−7.19 ± 13.42	
23–24.9	−8.08 ± 12.86	
≥ 25	−8.38 ± 12.99	
Smoking		< 0.01
Non-smoker	−7.02 ± 14.02	
Ex-smoker	−8.32 ± 12.36	
Current smoker	−9.56 ± 12.46	
Drinking		< 0.01
Non-drinker	−6.78 ± 13.03	
Moderate drinker	−8.34 ± 13.22	
Heavy drinker	−7.82 ± 12.77	
DM		< 0.01
No	−6.87 ± 12.54	
Yes	−27.37 ± 7.18	
HTN		< 0.01
No	−7.84 ± 13.13	
Yes	−10.79 ± 11.45	

Values are presented as mean ± standard deviation.
eGFR: estimated glomerular filtration rate; BMI: body mass index; DM: diabetes mellitus; HTN: hypertension.

Table 4. Adjusted OR for the effect of shift work on eGFR reduction

Work shift	Crude OR (95% CI)	Adjusted[a] OR (95% CI)
Daytime work	1.00	1.00
Shift work	2.61 (1.63–4.18)	4.07 (2.54–6.52)

eGFR: estimated glomerular filtration rate; OR: odds ratio; CI: confidence interval.
[a]Adjusted for sex, age, body mass index, smoking, drink, diabetes mellitus, and hypertension.

22–60 years in China; their results showed that individuals who had worked in shifts for >29 years had higher odds of a decrease in eGFR than did those with fixed daytime work schedules (OR: 1.37; 95% CI: 1.09–1.73). In Korea, Kang et al.[12] found that the prevalence of microalbuminuria among the women in their study was significantly higher for shift workers than for daytime workers (OR: 1.86; 95% CI: 1.02–3.39). In a study on manual laborers aged ≥ 20 years, Uhm et al. reported that the risk for CKD was significantly higher for female shift workers (OR: 2.04; 95% CI: 1.22–3.41).[13]

A previous animal study reported that disruption of the circadian rhythm can lead to kidney diseases[14] and how the kidneys play an important role in the biological circadian rhythm.[15,16] The circadian rhythm is generated internally but is synchronized by external factors such as light, foraging behavior, and temperature. Long-term exposure to a shortened light-dark cycle can affect physiological functions and increase the mortality rate in mice.[17] The suprachiasmatic nucleus (SCN) is the principal circadian clock in mammals, and neurons in the SCN help maintain the circadian rhythm over long periods.[18] The circadian clock in peripheral tissues is known as the peripheral clock. Irregular meal times resulting from shift work can disturb the renal circadian rhythm and consequently result in decreased GFR.[19]

Overall, the circadian rhythm plays an important role in maintaining homeostasis, and disruptions to this rhythm can have serious consequences for kidney function.[20]

Night shift workers have poor sleep quality or sleep deprivation. McMullan et al.[21] reported that an inadequate sleep duration induces a rapid decline in GFR, and Koch et al.[22] stated that a disruption in the sleep–wake cycle as a result of shift work exacerbates CKD. Sleep deprivation has also been shown to affect the nocturnal dip. In general, systolic and diastolic blood pressures rise in the morning, remain steady in the afternoon, and decline during nighttime sleep. Inadequate sleep hinders the normal decrease in blood pressure during nighttime sleep, and this increases the risk of chronic renal failure.[23] Additionally, Fu et al.[24] observed that elevated central and peripheral blood pressures are associated with decreased GFR. Elevated blood pressure and decreased arterial compliance may cause a reduction in GFR. Increased blood pressure increases the peripheral resistance, and altered blood flow to the kidneys damages the renal capillaries.[25] Moreover, blood pressure and arterial compliance are linked to vascular endothelial dysfunction, and an altered afferent arteriole pressure may be another mechanism underlying early renal injury.[26] Therefore, HTN may be an important contributor to diminished GFR in shift workers.

Psychosocial stress may be a facilitating factor for the effects of shift work on kidney diseases. Shift workers experience greater stress than do daytime workers.[27] Stress stimulates the sympathetic nervous system and causes renal vasoconstriction, which reduces renal blood flow and GFR. Furthermore, external stress from shift work continuously stimulates the hypothalamus–pituitary–adrenal axis, thereby activating the sympathetic nervous system. Activation of the sympathetic nervous system may influence renal function through the renin-angiotensin-aldosterone system (RAAS),[28] and an overactivated RAAS impairs renal function by increasing glomerular pressure, damaging vascular endothelial cells, and stimulating the production of reactive oxygen species.[29] The findings of previous studies and the present study indicate that disruption of the circadian rhythm and sleep deprivation resulting from shift work may significantly impair kidney function.

This study analyzed a study population of nearly 1.3 million over 5 years. However, there were a few limitations. First, although we performed a 5-year retrospective study, a longer period is considered necessary to examine the changes in GFR. Second, the data collected from questionnaire assessments may have been inaccurate, potentially increasing the risk of bias. Third, we only examined diagnoses of DM or HTN at the end of the observation period and did not examine the use of pharmacological therapy. The effects of pharmacological treatment for these chronic diseases on the prevention of CKD progress should be examined. Fourth, workers who are well-suited for long-duration shift work are more likely to have better physical health (healthy worker effect), which can result in an underestimation of the association between exposure and outcomes. Fifth, stress caused by shift work or changes in dietary patterns due to Shift work can also influence the decrease in glomerular filtration rate. However, due to limitations in the survey questions, these factors were not considered. Despite these limitations, This study showed an association between shift work and a decrease in glomerular filtration rate.

In further study, it is considered important to include factors such as health status, patterns of dietary changes, and stress levels. Additionally, conducting long-term studies that track changes in GFR over an extended period using a large sample size would allow for a more comprehensive comparison of changes over time.

CONCLUSIONS

This study investigated the effect of shift work on the decrease in eGFR and showed that the eGFR decrease in shift workers was significantly greater than that in daytime workers. However, this study was conducted on the basis of screening data, and further prospective studies are necessary to validate the results and identify measures to prevent CKD in shift workers.

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