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Original Article

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Investigation of Obstructive Sleep Apnea Using Portable Monitors and Health Check Data in Japanese Drivers

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Aims: The identification and appropriate management of commercial motor vehicle (CMV) drivers with unrecognized obstructive sleep apnea (OSA) is a major public health concern and priority; OSA among drivers has not been fully investigated in Japan, and a better understanding of this undiagnosed disease is warranted. Therefore, we evaluated the prevalence of OSA and the factors related to apnea−hypopnea index (AHI) in Japanese CMV drivers.

Methods: This retrospective study included 1309 Japanese CMV drivers aged 40−69 years. All the subjects received type Ⅳ portable sleep monitors (PMs) with Epworth Sleepiness Scale (ESS) and a periodic health check including anthropometrical and laboratory measurements, and a questionnaire of medical history, smoking status, and life style, following which variables related to AHI were analyzed.

Results: Of all the subjects, 23.9% had moderate to severe OSA (AHI ≥15). Age, body mass index (BMI), Log_eHbA1c and diastolic blood pressure (DBP) showed significance with AHI in 1309 subjects. The following factors were found to have significant odds ratio (OR) for AHI of ≥15 in 1309 subjects: age, ESS, DBP, and Log_eHbA1c.

Conclusion: Notably, drivers with undiagnosed OSA exist. In these subjects, AHI was related to obesity, hypertension, and diabetes. For the early diagnosis and intervention of OSA, BMI, blood pressure, and HbA1c measurements may be helpful, particularly for drivers. Furthermore, when performing an objective assessment of the suspected OSA, evaluating these parameters during routine medical check-ups may be useful and feasible in the detection of drivers with latent OSA.

Key words: Obstructive Sleep Apnea Syndrome, Sleep-Disordered Breathing, Occupational Health, Commercial motor vehicle drivers

Introduction

Till date, there have been only a few investigations of the relationship between obstructive sleep apnea (OSA) and Japanese commercial motor vehicle (CMV) drivers[1, 2], even though the identification, and appropriate management of CMV drivers with unrecognized OSA is a major public health concern and priority. Furthermore, it is well known that OSA leads to intermittent hypoxia, enhanced sympathetic activity, and increased oxidative stress[3]. Obesity is a major risk factor for snoring and sleep apnea, and most patients with OSA are overweight[4]. Previous reports have shown OSA to be associated with increased risk of hypertension[5, 6], stroke[7, 8], coronary artery disease[9, 10], insulin resistance[11, 12] and metabolic syndrome[13, 14].

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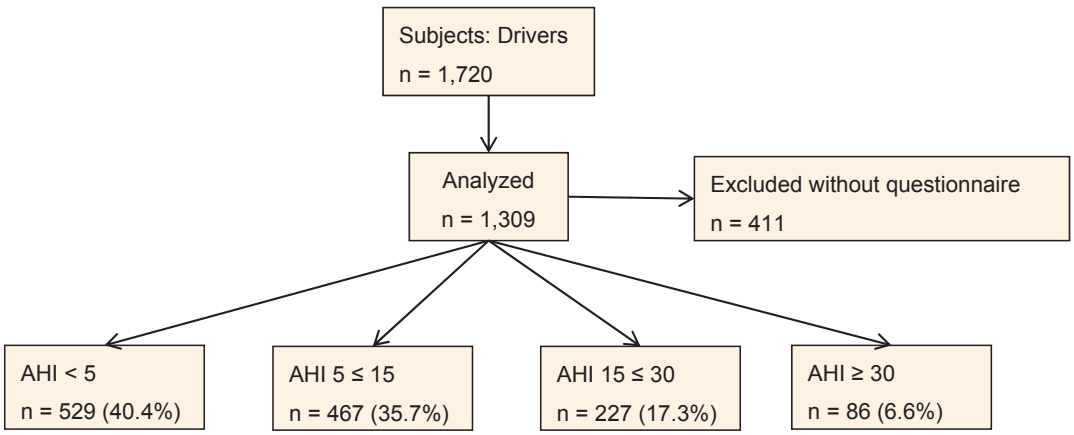

Fig. 1. Flow diagram of subject enrolment.

According to the health insurance association member rule in Japan, of the 1720 drivers, 1309 were required to answer the baseline questionnaire, and we analyzed data from these 1309 drivers regarding the relationship between AHI and questionnaire or measurement items. AHI = apnea−hypopnea index

Concerning traffic accidents, unintentionally falling asleep, nodding off while driving and having difficulty performing daily tasks because of sleepiness may all contribute to hazardous outcomes[15]. The National Department of Transportation estimates drowsy driving to be responsible for 1,550 fatalities and 40,000 nonfatal injuries annually in the United States[16]. In Japan, fatal traffic accidents of commercial transportation vehicles numbered 5448 cases in 2013[17]. Despite these accident reports documented by the government, epidemiological investigation on OSA in drivers has not yet been fully addressed in Japan. There may be many undiagnosed and untreated CMV drivers suffering from OSA and its related diseases, and these drivers may pose a risk to public safety. A better understanding of OSA in CMV drivers is therefore a major public health and trucking industry priority. As noted, it is essential that early diagnosis and intervention are required not only to reduce fatal traffic or industrial accidents but also for the drivers' health. Therefore, the aim of this study is to evaluate the prevalence of OSA and the factors associated with high apnea−hypopnea index (AHI) among 1309 Japanese drivers using type Ⅳ portable sleep monitors (PMs) and data from health check-ups.

Methods

Study Subjects

This cross-sectional study included professional CMV drivers working for a transport company in Japan. Between January 2011 and December 2014, 1720 drivers working at the company randomly received type Ⅳ PMs between January 2011 and December 2014 with the Epworth Sleepiness Scale (ESS), as described below. We analyzed PMs' data together with periodic health check data that included a specific questionnaire, anthropometrical measurements, and laboratory assessments. Because of health insurance association membership regulations in Japan, 1309 of the 1720 drivers were required to complete a specific questionnaire and those 1309 drivers were analyzed in this study (**Fig. 1**). Most study subjects were men and only 22 (1.68%) women were included. The age distribution was as follows: 47.7% were aged 40−49 years, 38.6% were aged 50−59 years and 13.7% were aged ≥60 years. No subject had been diagnosed with, or had received treatment for sleep apnea. Informed consent was obtained from all participants by comprehensive agreement. The institutional review board of our hospital approved this study (#17002), which was conducted in accordance with the principles of the Declaration of Helsinki.

Measurements

The principal objective of this study was to assess the relationship between OSA severity (measured categorically using the AHI) and anthropometric, clinical, and laboratory data obtained from nationwide specific health check-up data. The modified Japanese version of the ESS[18] was used to assess subjective sleepiness. The subjects also completed specific questionnaire that covered their current and past medical history, their smoking status, and whether they had gained ≥10 kg in weight since the age of 20 years. A current smoker was defined as a subject who smokes ≥100 cigarettes or who has smoked for at least 6 months and in the last month. Trained nurse staff measured their height, weight, waist circumference at the level of the navel, and systolic

and diastolic blood pressure using an automated digital blood pressure monitor (BP-103i II; Omron Healthcare, Kyoto, Japan). Subjects were required to fast for 10 h or for as long as possible. Finally, fasting and nonfasting blood samples were obtained from 496 (37.9%) and 813 (62.1%) subjects, respectively. As part of the periodic mandatory workplace health check-up, venous blood was drawn at 15 branch offices of the company where the drivers work. Serum triglyceride level was measured using an enzymatic method (free glycerol-eliminated method). LDL- and HDL cholesterol were measured using a direct method with an automatic analyzer (TBA-c1600, Toshiba Medical Systems Corporation, Tochigi, Japan). HbA1c was measured using a HPLC method with an automatic analyzer (HLC-723®G8, Tosoh Corporation, Tokyo, Japan) at our hospital. Proteinuria was coded as (−), (±), (1+), (2+), and (≥3+), and positive proteinuria was defined as ≥1+. Other laboratory parameters were measured using specific health check-up data, and we investigated the relationship between AHI and these measurements.

Sleep Study

All subjects underwent a nocturnal, unattended sleep study at home using a type IV, 4-channel PM (SAS-2100; Nihon Kohden Co. Ltd., Tokyo, Japan) for one night. This recorded four physiological parameters: snoring, oxygen saturation (SpO_2), heart rate (via a probe taped to a finger) and airflow (via a nasal pressure transducer). The device did not monitor body posture. The instructions for use illustrated the correct placement of the monitor. No specific limitations on daily life were imposed on the monitoring day; alcohol consumption was allowed in moderation. The subjects were asked to indicate the time they went to bed and the time they awoke the following morning. Our subsequent analysis was based on the automatic report from the accompanying software (QP-021W; Nihon Kohden), which analyzed the recording and presented the data. The expenses of PMs were borne by the transport company.

Respiratory events were scored according to the American Academy of Sleep Medicine criteria[19]. The oxygen desaturation index (ODI) was defined by the number of arterial oxygen saturation dips (≥3%) per hour of examination. Apnea events were defined as cessation of airflow for ≥10 s and hypopnea as a decrease of ≥50% from baseline in the amplitude of the nasal cannula airflow for ≥10 s during sleep associated with oxygen desaturation ≥3%. The AHI score was calculated from the number of apnea and hypopnea events per hour, using the total recording time as the denominator, and categorized as no sleep apnea (<5), or mild (5−14.9), moderate (15−29.9) or severe (≥30) sleep apnea. Several studies have demonstrated a high sensitivity and specificity of the laboratory type IV portable monitor AHI compared with the AHI from the simultaneous PSG study at all AHI levels, at an AHI of ≥15 events per h (sensitivity, 91% and specificity, 95%; sensitivity, 100% and specificity, 92%, respectively)[20, 21]. The AHI comparison from the home IV portable monitor and laboratory PSG studies has also demonstrated good sensitivity and specificity at AHI levels of ≥5 (sensitivity, 81% and specificity, 77%; sensitivity, 92% and specificity, 77%, respectively) and at ≥15 events per h (sensitivity, 67% and specificity, 91%; sensitivity, 73% and specificity, 85%, respectively)[21, 22].

Statistical Analysis

Data are expressed as mean±SD, median (interquartile range) or percentage for the parametric, nonparametric, and categorical data, respectively. Because of skewed distribution, GOT, GPT, γ-GTP, TG, and HbA1c values were logarithmically transformed before the analysis. Baseline characteristics were compared between the four AHI categories using ANOVA with *post hoc* Tukey analysis, Kruskal−Wallis, and chi-squared tests for parametric, nonparametric, and categorical variables, respectively. Correlations between AHI and demographic, anthropometric, and laboratory variables were assessed by Pearson's correlation coefficients. We included age, BMI, ESS, DBP, Log_eGPT, Log_eHbA1c, and HDL-C in the multiple linear regression analysis using stepwise selection to evaluate AHI with each parameter. Multivariate logistic regression analysis was applied by adjusting for important AHI factors in univariate analyses, which were age, ESS, BMI, DBP, smoking history, body weight change, HDL-C, Log_eGPT, and Log_eHbA1c using forced entry. Adjusted odds ratios (ORs) were estimated with 95% confidence interval (CI), referencing to that for participants with AHI of <15. All statistical tests were two-tailed and a *p*-value of <0.05 was considered statistically significant. SPSS version 22 software (IBM Corp., Armonk, NY, USA) was used for the analyses.

Results

Descriptive characteristics of the subjects and the distributions of the covariates, stratified by the four AHI categories, are presented in **Table 1**. The mean age of the 1309 drivers was 49.73±6.77 years, 98.3% were men, and the median body mass index (BMI) was 23.9 kg/m^2. According to the AHI scores, 40.4% of the subjects did not have OSA (AHI <5), whereas 23.9% had moderate to severe OSA (AHI ≥15). Those with more severe AHI were more obese and had a greater burden of cardiometabolic medication intake

Table 1. Demographic, clinical, and sleep monitor data categorized by the severity of apnea−hypopnea index*

	Total population	AHI categories			
	0−5	5≤15	≤15	≤30	*p*-value
Number (%)	1309 (100)	529 (40.4)	467 (35.7)	227 (17.3)	86 (6.6)	
Age (years)	49.73±6.77	48.96±6.82	49.83±6.71	50.55±6.62	51.85±6.57	<0.001
AHI	6.7 (2.8−14.3)	2.2 (1.1−3.4)	8.3 (6.6−11.2)	20.4 (17.4−24.7)	38.7 (33.0−49.0)	<0.001
ODI (3%)	6.9 (3.2−13.4)	2.7 (1.5−4.0)	8.4 (6.6−10.9)	19.4 (16.1−22.9)	36.3 (30.5−47.1)	<0.001
ESS	5 (3−8)	5 (3−8)	5 (3−7)	6 (3−8)	5 (3−8)	0.094
BMI (kg/m^2)	23.9 (22−26.1)	22.6 (20.95−24.4)	24 (22.5−26.2)	25.8 (23.5−28.3)	26.6 (24.6−30.4)	<0.001
WC (cm)	86 (80−92)	82 (77−87)	87 (82−92)	90 (85−96)	93 (87−102)	<0.001
SBP (mmHg)	128.47±14.93	125.45±14.83	128.6±14.04	132.98±14.74	134.45±16.06	<0.001
DBP (mmHg)	79.82±10.55	77.52±10.65	80.07±9.74	83.37±10.01	83.23±11.90	<0.001
WBC (/μL)	6710 (5670−8085)	6610 (5570−7990)	6770 (5620−8040)	6810 (5860−8360)	6910 (6005−8497)	0.056
Hb (g/dL)	15.33±1.10	15.26±1.10	15.30±1.10	15.42±1.12	15.66±1.05	0.009
Ht (%)	45.20±3.13	45.02±3.14	45.14±3.20	45.43±3.05	46.08±2.79	0.019
GOT (IU/L)	21 (18−26)	21 (17−26)	21 (8−26)	22 (19−28)	22 (18−32)	0.009
Log$_e$GOT (IU/L)	3.1±0.35	3.07±0.31	3.11±0.39	3.15±0.34	3.18±0.4	0.004
GPT (IU/L)	22 (16−33)	21 (15−30)	22 (16−34)	26 (20−38)	28.5 (19−46)	<0.001
Log$_e$GPT (IU/L)	3.18±0.54	3.07±0.49	3.18±0.57	3.33±0.52	3.42±0.59	<0.001
Cre (mg/dL)	0.9 (0.8−0.98)	0.9 (0.8−0.98)	0.9 (0.8−0.99)	0.9 (0.8−1)	0.9 (0.8−0.99)	0.315
γGTP (IU/L)	37 (24−59)	32 (22−54)	38 (25−59)	43 (29−63)	43.5 (31−64)	<0.001
Log$_e$γGTP (IU/L)	3.69±0.67	3.6±0.69	3.7±0.67	3.81±0.62	3.80±0.56	<0.001
TG (mg/dL)	134 (90−202)	124 (81.5−179.0)	139 (94−213)	148 (102−219)	161 (117−221)	<0.001
Log$_e$TG (mg/dL)	4.93±0.59	4.82±0.59	4.97±0.59	5.04±0.58	5.08±0.49	<0.001
HDL−C (mg/dL)	55.65±14.20	58.01±14.46	54.96±14.54	53.04±13.08	51.78±11.05	<0.001
LDL−C (mg/dL)	128.4±32.65	125.64±30.96	130.48±33.48	128.29±34.12	134.93±33.11	0.028
UA (mg/dL)	5.94±1.27	5.75±1.21	6.08±1.28	6.08±1.35	6.09±1.26	<0.001
HbA1c (%)	5.6 (5.4−5.9)	5.5 (5.4−5.8)	5.6 (5.4−5.9)	5.8 (5.5−6.2)	5.8 (5.5−6.3)	<0.001
Log$_e$HbA1c (%)	1.75±0.12	1.73±0.10	1.75±0.11	1.80±0.17	1.79±0.12	<0.001
ESS ≥11 (+) (%)	119 (9.1)	44 (8.3)	36 (7.7)	29 (12.8)	10 (11.6)	0.119
Weight gain (>10 kg) (+) (%)	632 (48.3)	175 (33.1)	250 (53.5)	143 (63.0)	64 (74.4)	<0.001
Current smoking (+) (%)	525 (40.1)	219 (41.4)	184 (39.4)	87 (38.3)	35 (40.7)	0.855
Everyday drinking (+) (%)	343 (26.2)	125 (23.6)	129 (27.6)	63 (27.8)	26 (30.2)	0.347
Proteinuria (1+, 2+) (%)	42 (3.2)	10 (1.9)	12 (2.6)	12 (5.3)	8 (9.3)	0.001
Antihypertensive medicine intake (%)	255 (19.5)	64 (12.1)	95 (20.3)	61 (26.9)	35 (40.7)	<0.001

(Cont Table 1)

	Total population	AHI categories			
		0–5	5≤15	≤15	≤30	*p*-value
Antidiabetic medicine intake (%)	75 (5.7)	16 (3.0)	25 (5.4)	23 (10.1)	11 (12.8)	<0.001
Antihyperlipidemic medicine intake (%)	114 (8.7)	30 (5.7)	40 (8.6)	32 (14.1)	12 (14.0)	0.001
Brain stroke past history (+) (%)	8 (0.6)	2 (0.4)	3 (0.6)	2 (0.9)	1 (1.2)	0.757
History of angina or MI (+) (%)	19 (1.5)	6 (1.1)	6 (1.3)	4 (1.8)	3 (3.5)	0.375
History of CRF or dialysis (+) (%)	1 (0.1)	0 (0)	0 (0)	1 (0.4)	0 (0)	0.189
Cancer history (+) (%)	9 (0.7)	5 (0.9)	1 (0.2)	2 (0.9)	1 (1.2)	0.483

*Unless otherwise stated, data are presented as mean ± SD, median (interquartile range) or n (%).
AHI = apnea–hypopnea index; ODI = oxyhemoglobin desaturation index; ESS = Epworth sleepiness scale; BMI = body mass index; WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; WBC = white blood cell; Hb = hemoglobin; Ht = hematocrit; GOT = glutamic oxalacetic transaminase; GPT = glutamic pyruvic transaminase; Cre = creatinine; γGTP = gamma-glutamyl transpeptidase; TG = triglycerides; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; UA = uric acid; HbA1c = glycosylated hemoglobin; MI = myocardial infarction; CRF = chronic renal failure

than those with normal and mild OSA. There was no significant difference in ESS between the AHI categories, but glycosylated hemoglobin (HbA1c) (%) varied significantly ($p<0.001$).

In the univariate analysis, AHI correlated significantly with factors other than ESS and Cre in the 1309 subjects. Additional analysis excluding subjects with antihypertensive, antidiabetic, and hyperlipidemic medicine intake was performed; the results were similar to those of all the 1309 subjects (**Table 2**).

A multiple linear regression analysis using stepwise selection was constructed with variables showing significance with AHI in univariate analysis. Age, BMI, Log_eHbA1c and DBP showed significance with AHI in 1309 subjects (age: standardized $\beta=0.13$, $p<0.001$; BMI: $\beta=0.38$, $p<0.001$; Log_eHbA1c: $\beta=0.072$, $p=0.006$; DBP: $\beta=0.073$, $p=0.006$). Furthermore, when subjects with antihypertensive, antidiabetic, and hyperlipidemic medicine intake were excluded, age, BMI and Log_eHbA1c showed significance with AHI in all the models (**Table 3**).

In multivariate logistic analysis, after adjustment for age, ESS, BMI, DBP, smoking history, body weight change, HDL-C, Log_eGPT, and Log_eHbA1c, the following factors were found to have significant ORs for AHI ≥15 in 1309 subjects: age (OR 1.048, 95% CI 1.026–1.071, $p<0.001$); ESS (OR 1.055, 95% CI 1.015–1.096, $p=0.006$); BMI (OR 1.192, 95% CI 1.134–1.254, $p<0.001$); DBP (OR 1.023, 95% CI 1.009–1.038, $p=0.001$); Log_eHbA1c (OR 6.512, 95% CI 2.219–19.115, $p<0.001$) (**Table 4**). In addition, in the models excluding antihypertensive, antidiabetic, and hyperlipidemic medicine intake, the result was similar with that in all the 1309 subjects.

Discussion

The interesting point of this study is a large sample to examine OSA and health check data among professional drivers, which provides a more real situation of OSA severity and related status.

A major finding in our study was the 23.9% prevalence of moderate and severe OSA (AHI ≥15) among drivers aged 40–69 years. The prevalence of OSA in the general population varies across the world. These differences could be due to different monitoring methods and definitions for the apnea hypopnea scoring, as well as differences in study design and populations[23-27]. In a previous study on 1313 Japanese drivers aged 40–69 years, the prevalence of 3% ODI ≥15, as assessed by pulse oximetry, was 8.5%[1]. Compared with that, our study subjects showed higher AHI scores and were older, although the mean BMI was similar. Furthermore, 35% of our subjects had BMI ≥25 compared with 31.6% of the Japanese population aged 20–69 years[28]. Therefore, considering the prevalence of obesity, our results showed that there may also be a much greater prevalence of undiagnosed (latent) OSA in the general Japanese population, than what we assumed.

Another important finding was that HbA1c also had a significant association with AHI scores (OR 6.512, 95% CI 2.219–19.115, $p<0.001$) as shown in the previous studies[29, 30]. However, the strength of this study is that we found these correlations particularly in drivers. In previous reports, OSA has been linked to the progression of diabetes independent of obesity, via activation of the sympathetic nervous system[31]. In other reports, cross-sectional estimates from clinical populations and population studies have suggested that

Table 2. Pearson correlation coefficients of AHI with demographic, clinical, and anthropometric factors

Total			Model 1		
Variable	C.C (r)	*p*-value	Variable	C.C (r)	*p*-value
ODI (3%)	0.98	< 0.001	ODI (3%)	0.977	< 0.001
BMI (kg/m^2)	0.409	< 0.001	BMI (kg/m^2)	0.382	< 0.001
WC (cm)	0.388	< 0.001	WC (cm)	0.356	< 0.001
DBP (mmHg)	0.209	< 0.001	Log$_e$GPT (IU/L)	0.208	< 0.001
Log$_e$GPT (IU/L)	0.208	< 0.001	DBP (mmHg)	0.208	< 0.001
SBP (mmHg)	0.207	< 0.001	Log$_e$HbA1c (%)	0.207	< 0.001
Log$_e$HbA1c (%)	0.193	< 0.001	SBP (mmHg)	0.206	< 0.001
Log$_e$TG (mg/dL)	0.146	< 0.001	HDL-C (mg/dL)	−0.154	< 0.001
HDL-C (mg/dL)	−0.141	< 0.001	Log$_e$TG (mg/dL)	0.151	< 0.001
Age	0.116	< 0.001	UA (mg/dL)	0.122	< 0.001
Log$_e$ γ-GTP (IU/L)	0.113	< 0.001	Age	0.116	< 0.001
Log$_e$GOT (IU/L)	0.111	< 0.001	Log$_e$ γ-GTP (IU/L)	0.112	< 0.001
Hb (g/dL)	0.094	0.001	Hb (g/dL)	0.105	0.001
UA (mg/dL)	0.093	0.001	Log$_e$GOT (IU/L)	0.102	0.001
Ht (%)	0.091	0.001	Ht (%)	0.099	0.001
WBC (/μL)	0.087	0.002	WBC (/μL)	0.088	0.004
LDL-C (mg/dL)	0.067	0.015	LDL-C mg/dL	0.073	0.018
ESS	0.038	0.17	ESS	0.045	0.144
Cre (mg/dL)	0.029	0.301	Cre (mg/dL)	0.031	0.314

Model 2			Model 3		
Variable	C.C (r)	*p*-value	Variable	C.C (r)	*p*-value
ODI (3%)	0.979	< 0.001	ODI (3%)	0.979	< 0.001
BMI (kg/m^2)	0.397	< 0.001	BMI (kg/m^2)	0.4	< 0.001
WC (cm)	0.371	< 0.001	WC (cm)	0.378	< 0.001
Log$_e$GPT (IU/L)	0.213	< 0.001	SBP (mmHg)	0.206	< 0.001
DBP (mmHg)	0.207	< 0.001	Log$_e$GPT (IU/L	0.199	< 0.001
SBP (mmHg)	0.19	< 0.001	DBP (mmHg)	0.198	< 0.001
Log$_e$HbA1c (%)	0.185	< 0.001	Log$_e$HbA1c(%)	0.191	< 0.001
HDL-C (mg/dL)	−0.147	< 0.001	Log$_e$TG (mg/dL)	0.148	< 0.001
Log$_e$TG (mg/dL)	0.14	< 0.001	HDL-C (mg/dL)	−0.13	< 0.001
Log$_e$ γ-GTP(IU/L)	0.122	< 0.001	Age	0.128	< 0.001
UA (mg/dL)	0.113	< 0.001	Log$_e$ γ-GTP (IU/L)	0.119	< 0.001
Age	0.111	< 0.001	Log$_e$GOT (IU/L)	0.092	0.001
Log$_e$GOT (IU/L)	0.11	< 0.001	LDL-C (mg/dL)	0.085	0.003
Hb (g/dL)	0.089	0.002	WBC (/μL)	0.085	0.003
WBC (/μL)	0.085	0.003	UA (mg/dL)	0.083	0.004
Ht (%)	0.085	0.003	Hb (g/dL)	0.077	0.008
Cre mg/dL	0.067	0.019	Ht (%)	0.076	0.008
LDL-C (mg/dL)	0.058	0.041	ESS	0.04	0.166
ESS	0.046	0.109	Cre (mg/dL)	0.002	0.954

In Model 1, 1054 subjects who do not take antihypertensive medicine were included. In Model 2, 1234 subjects who do not take antidiabetic medicine were included. In Model 3, 1195 subjects who do not take hyperlipidemic medicine were included.
C.C = correlation coefficient, AHI = apnea–hypopnea index; ODI = oxyhemoglobin desaturation index; BMI = body mass index; WC = waist circumference; HbA1c = glycosylated hemoglobin; GPT = glutamic pyruvic transaminase; SBP = systolic blood pressure; DBP = diastolic blood pressure; TG = triglyceride; γ-GTP = gamma-glutamyl transpeptidase; HDL-C = high-density lipoprotein cholesterol; WBC = white blood cell; GOT = glutamic oxalacetic transaminase; Hb = hemoglobin; UA = uric acid; Ht = hematocrit; LDL-C = low-density lipoprotein cholesterol; Cre = creatinine; ESS = Epworth sleepiness scale

Table 3. Multivariate regression analysis of relationship of anthropometric, clinical and laboratory factors with AHI*

	Total, 1309 Adjusted $R^2=0.197$			Model 1 Adjusted $R^2=0.181$		
	standard β	95% CI	*p*-value	standard β	95% CI	*p*-value
Age	0.13	0.132−0.301	<0.001	0.121	0.1−0.275	<0.001
BMI (kg/m^2)	0.38	1.018−1.350	<0.001	0.343	0.827−1.177	<0.001
Log_eHbA1c (%)	0.072	1.952−11.564	0.006	0.103	3.92−13.948	<0.001
DBP (mmHg)	0.073	0.023−0.134	0.006	0.082	0.023−0.134	0.006
Log_eGPT	N.A	N.A	N.A	N.A	N.A	N.A

	Model 2 Adjusted $R^2=0.187$			Model 3 Adjusted $R^2=0.190$		
	standard β	95% CI	*p*-value	Standard β	95% CI	*p*-value
Age	0.135	0.133−0.304	<0.001	0.151	0.162−0.332	<0.001
BMI (kg/m^2)	0.347	0.889−0.255	<0.001	0.394	1.048−1.374	<0.001
Log_eHbA1c (%)	0.066	1.715−14.838	0.013	0.077	2.355−12.717	0.004
DBP (mmHg)	0.061	0.007−0.119	0.028	N.A	N.A	N.A
Log_eGPT	0.063	0.118−2.431	0.031	N.A	N.A	N.A

*We included age, BMI, ESS, DBP, HDL-C, Log_eHbA1c and Log_eGPT into the multiple linear regression analysis by stepwise selection.
AHI=apnea−hypopnea index; BMI=body mass index; ESS=Epworth sleepiness scale; HbA1c=glycosylated hemoglobin; DBP=diastolic blood pressure; GPT=glutamic pyruvic transaminase; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; N.A.=not applicable
In Model 1, 1054 subjects who do not take antihypertensive medicine were included. In Model 2, 1234 subjects who do not take antidiabetic medicine were included. In Model 3, 1195 subjects who do not take hyperlipidemic medicine were included.

up to 40% of people with OSA have diabetes[32, 33]. Likewise, in people who are known to have diabetes, the prevalence of OSA may be as much as 23%[34]. HbA1c measurement has recently been approved of as a standalone test for type 2 diabetes by the American Diabetes Association[35], an accurate predictor of future type 2 diabetes and a better predictor of future cardiovascular illness and death than fasting plasma glucose[36]. Of note, we would suggest that our data support the use of HbA1c as an effective, convenient, and inexpensive tool in drivers to identify diabetes earlier. Moreover, HbA1c is not affected by the dietary intake state and is feasible; therefore, we consider HbA1c to be a good comorbidity marker of diabetes in OSA drivers. Altogether, patients with moderate to severe OSA should always be warned with regard to the complications of diabetes in day-to-day medical examinations by health professionals.

Another remarkable finding was that only 120 subjects (9.17%) had ESS scores ≥11. Most of the subjects did not recognize subjective sleepiness and we presume that subjective self-reports require close attention in their interpretation. In previous studies in general settings, various types of questionnaires lacked sufficient sensitivity and specificity to replace a sleep study in diagnosing OSA[37]. In particular, self-reporting appeared to be less reliable in an occupational setting[38]. Every driver should therefore be required to undergo an objective physical examination such as BMI or blood pressure measurement as included in the Federal Motor Carrier Safety Administration standards[39] and should be subjected to an accessible and feasible sleep study with PMs, even if there remain many unresolved issues with regard to PMs.

There are some important limitations in this study. First, almost all subjects were Japanese men and there were only a few women among drivers at a single company; therefore, the present findings may not be applicable to the general population, especially women. There are reports that the risk of OSA is less in women than in men before menopause, but women still experience more sleep problems than men[40]; therefore, for validation in the general population, further research using PMs and health check data would be required to evaluate the heterogeneous group. Second, type IV PMs provide nasal airflow, oxygen saturation, and pulse information, but do not provide data related to sleep stages and body positioning unlike the standard PSG. Considering that PMs generally use recording time rather than total actual sleep time, the AHI obtained

Table 4. Odds ratios (OR) and 95% confidence intervals (CIs) of each independent variable for AHI ≥15 by multivariate logistic regression analysis*

	Total, 1309		Model 1	
Variables	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.048 (1.026−1.071)	<0.001	1.049 (1.022−1.077)	<0.001
ESS	1.055 (1.015−1.096)	0.006	1.056 (1.011−1.103)	0.015
BMI (kg/m^2)	1.192 (1.134−1.254)	<0.001	1.147 (1.079−1.219)	<0.001
DBP (mmHg)	1.023 (1.009−1.038)	0.001	1.024 (1.007−1.040)	0.004
Smoking	0.895 (0.669−1.196)	0.452	0.952 (0.678−1.336)	0.775
Body weight change	1.264 (0.918−1.739)	0.151	1.453 (0.995−2.121)	0.053
HDL-C (mg/dL)	1.001 (0.989−1.013)	0.883	0.994 (0.98−1.007)	0.367
Log$_e$GPT (IU/L)	1.246 (0.946−1.642)	0.117	1.328 (0.945−1.865)	0.102
Log$_e$HbA1c (%)	6.512 (2.219−19.115)	0.001	8.184 (2.307−29.029)	0.001
	Model 2		Model 3	
Variables	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.049 (1.026−1.073)	<0.001	1.051 (1.027−1.076)	<0.001
ESS	1.058 (1.017−1.100)	0.005	1.057 (1.016−1.100)	0.006
BMI (kg/m^2)	1.199 (1.136−1.266)	<0.001	1.171 (1.110−1.236)	<0.001
DBP (mmHg)	1.020 (1.005−1.035)	0.008	1.020 (1.005−1.035)	0.009
Smoking	0.861 (0.634−1.168)	0.335	0.834 (0.611−1.139)	0.255
Body weight change	1.230 (0.875−1.729)	0.234	1.303 (0.929−1.828)	0.125
HDL-C (mg/dL)	0.998 (0.986−1.010)	0.726	1.000 (0.988−1.012)	0.961
Log$_e$GPT (IU/L)	1.308 (0.976−1.753)	0.072	1.335 (0.988−1.804)	0.06
Log$_e$HbA1c (%)	9.260 (1.93−4.431)	0.005	9.230 (2.736−31.134)	<0.001

*Adjusted for age, ESS, BMI, DBP, smoking history (never, former or current), body weight change ≥10 kg gain since the age of 20 years (yes/no), HDL-C, Log$_e$GPT and Log$_e$HbA1c.

AHI=apnea−hypopnea index; ESS=Epworth sleepiness scale; BMI=body mass index; DBP=diastolic blood pressure; HDL-C=high-density lipoprotein cholesterol; GPT=glutamic pyruvic transaminase; HbA1c=glycosylated hemoglobin.

Multivariate logistic regression was applied using forced entry, adjusting for factors identified to be important for AHI in univariate analyses, which included age, ESS score, BMI, DBP, smoking history, body weight change, HDL-C, Log$_e$GPT, and Log$_e$HbA1c. Adjusted odds ratios were estimated with 95% confidence interval (CI), referencing to that for subjects with AHI <15.

In Model 1, 1054 subjects who do not take antihypertensive medicine were included. In Model 2, 1234 subjects who do not take antidiabetic medicine were included. In Model 3, 1195 subjects who do not take hyperlipidemic medicine were included.

from PMs tends to underestimate the severity of sleep apnea compared with AHI by PSG. This means our cohort may have included drivers with more severe OSA, and further prospective randomized studies that directly compare various PMs and types of PSG will be important in the appropriate validation of PMs for CMV drivers. Third, the subjects included CMV drivers who are not at high risk of having OSA, because the transport company independently and equally conducted PM studies for all the CMV drivers in our study without any bias. According to the guidelines, the use of PMs can be considered for those deemed to be at a high risk of having OSA without any severe comorbidities[41]. However, as observed in our study results, there exists undiagnosed OSA at a certain proportion. We therefore consider it very important to identify OSA patients using objective measures such as PMs, although there are many difficulties in clarifying the optimal algorithm and results interpretation in testing OSA using PMs among drivers.

Conclusion

Our findings suggest that there exists a certain proportion of undiagnosed, mild to severe OSA in CMV drivers in Japan. Moreover, HbA1c was strongly associated with AHI, independent of age and obesity. From a practical standpoint, OSA drivers are always to be warned about the complication of hypertension or diabetes by the industrial or attending physician. Conversely, using periodic health check data, our study proposes that obesity, hypertension, and HbA1c eleva-

tion may indicate latent OSA in CMV drivers. Further prospective studies to examine the long-term causal relationship between OSA and metabolic and cardiovascular disease complications are required for the prevention and early diagnosis of OSA in Japanese drivers.

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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