

The Aging Male



ISSN: (Print) (Online) Journal homepage: informahealthcare.com/journals/itam20

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To cite this article: Sachiko Kubo, Toshiyuki Yasui, Yukie Matsuura & Masahito Tomotake (2020) Differences in male climacteric symptoms with aging among rotating night shift workers, The Aging Male, 23:5, 995-1003, DOI: 10.1080/13685538.2019.1650264

To link to this article: https://doi.org/10.1080/13685538.2019.1650264

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ORIGINAL ARTICLE



Differences in male climacteric symptoms with aging among rotating night shift workers

Sachiko Kubo^{a,b}, Toshiyuki Yasui^c, Yukie Matsuura^c and Masahito Tomotake^d

^aGraduate School of Health Sciences, Tokushima University, Tokushima, Japan; ^bFaculty of Nursing, Shikoku University, Tokushima, Japan; ^cDepartment of Reproductive and Menopausal Medicine, Tokushima University Graduate School, Tokushima, Japan; ^dDepartment of Mental Health, Tokushima University Graduate School, Tokushima, Japan

ABSTRACT

Objective: The aim of this study was to clarify the actual status of male climacteric symptoms in rotating night shift workers and how to cope with the symptoms.

Methods: We planned a self-administered questionnaire survey in male rotating night shift workers. Male climacteric symptoms were evaluated by using the Aging Males' Symptoms (AMS) scale.

Results: Of 1891 questionnaires that were sent, 1561 were collected. There were significant differences in total AMS scores among the age groups. In all age groups, there were high proportions of men with increased need for sleep and often feeling tired (64.9%) and decrease in muscular strength (60.7%). There were significant differences in AMS scores for somatic symptoms between men in their 20 s and those in their 40 s or 50 s and between men in their 30 s and those in their 50 s and in AMS scores for sexual symptoms between men in their 20 s and those in their 30 s, 40 s, 50 s or 60 s, between men in their 30 s and those in their 40 s and those in their 50 s or 60 s.

Conclusion: Significant age-dependent differences are found in somatic symptoms and sexual symptoms in rotating night shift workers.

ARTICLE HISTORY

Received 22 April 2019 Revised 27 July 2019 Accepted 27 July 2019 Published online 8 August 2019

KEYWORDS

Male climacteric symptoms; aging males' symptoms (AMS) scale; middle-aged men; rotating night shift workers

Introduction

Late-onset hypogonadism (LOH) syndrome, which causes various symptoms due to a decrease in androgen, is generally called male climacteric symptoms. Recently, LOH syndrome has received much attention worldwide [1]. The onset and duration of LOH syndrome differ greatly among individuals. Various symptoms in LOH syndrome have been classified as somatic symptoms such as general fatigue, psychological symptoms such as decrease in vitality, and sexual symptoms such as decrease in libido. LOH syndrome has been extensively evaluated by using the Aging Males' Symptoms (AMS) scale. Among 499 men aged from 40 to 90 years who visited a hospital in Indonesia, 54.5% had mild, 39.0% had moderate and 6.5% had severe AMS levels [2]. The effects of hormone treatment in 261 patients with LOH syndrome were investigated by using AMS scale in Germany [3]. Among 103 Iranian men aged 40-76 years, 73.6% of the men experienced symptoms of andropause and the proportions of men who had mild, moderate and

severe AMS scores were 38.6%, 27.1% and 7.9%, respectively [4]. In Japan, the actual status of male climacteric symptoms has been examined after medical examinations and treatment for male climacteric symptoms were started in 2000. Ichioka et al. [5] also reported that the proportions of men with a mild AMS score were 42.9% in men in their 30 s, 51.2% in men in their 40 s, 61.7% in men in their 50 s and 72.6% in men in their 60 s among 206 healthy men.

In terms of occupational health, it is important to consider physical health and mental health of workers, particularly night shift workers. Accordance to the United States Bureau of Labor Statistics in 2004, 14.8% of the labor force was shift workers and 70% of the shift workers were night shift workers [6]. According to the Japanese Ministry of Health, Labor and Welfare, the proportion of night shift workers in 2005 was 34.1% (manufacturing: 25.2%), and it increased to 36% in 2010 (manufacturing: 30.4%) in companies in which the number of employees was more than 10 [7]. It has been reported that night shift work was associated with various health problems including cardiovascular

diseases, gastrointestinal disturbances and metabolic syndrome [8-12]. Kaneko et al. [13] reported that the proportion of male workers with a depressive state was higher in double shift workers than in day shift workers. Male climacteric symptoms might occur due to androgen deficiency in rotating night shift workers who have mental health disturbances. Physical and psychological management is necessary for shift workers. From the viewpoint of industrial health, Horie [14] reported that the quality of life will decrease for men with LOH syndrome who do not receive treatment. Since the proportion of rotating night shift workers has been increasing, it is important for such workers to voluntarily visit a hospital for examination and treatment of LOH syndrome. However, the actual status of male climacteric symptoms in rotating night shift workers and how the workers cope with the symptoms have not been reported.

The aim of this study was to clarify the actual status of male climacteric symptoms in rotating night shift workers and to determine the relationship between symptoms and age.

Subjects and methods

We planned an unsigned self-administered questionnaire survey in male rotating night shift workers over the age of 20 years, including those working all or some of the hours from 10 pm to 5 am, in manufacturing companies. We asked the managers of general affairs or occupational nurses in 33 companies and distributed the questionnaires to 1891 male rotating night shift workers throughout Japan during the period from March to May in 2017. The questionnaires were collected from collection boxes or by mail.

The demographic characteristics in the questionnaire were age, work experience, length of service in shift work, type of shift, lifestyle (diet, physical activity, smoking habit, alcohol consumption, sleeping status, ways of spending free time), degree of stress, recognition of andropause and awareness of male climacteric symptoms, and coping strategy. Male climacteric symptoms were evaluated by using the AMS scale. The AMS questionnaire, which is a self-administered questionnaire that was developed in Germany, has been used worldwide for assessing male climacteric symptoms [4,15–17]. The questionnaire consists of 17 items including seven items for somatic symptoms, five items for psychological symptoms and five items for sexual symptoms. The AMS scale is a self-rated scale of the degrees of symptoms and each answer is rated with a 5-point Likert-type scale ranging from 1

(none) to 5 (very severe). A total score of less than 26 and less indicates no symptoms, a total score of more than 27 and less than 36 indicates mild symptoms, a total score of more than 37 and less than 49 indicates moderate symptoms, and a total score of 50 or higher indicates severe male climacteric symptoms [15–16]. AMS was translated into Japanese and its reliability has been verified for validity [17].

Statistical analysis

Baseline characteristics were analyzed by descriptive statistics. We classified male climacteric symptoms into four groups according to the degree of symptoms (none, mild, moderate, severe) and performed analysis for five generations (20 s, 30 s, 40 s, 50 s and 60 s). We used the chi-square test for comparing the proportions of subjects with each symptom among the age groups. Assuming that AMS score does not follow the normal distribution, we compared AMS scores among the age groups by using the Kruskal–Wallis test. The Bonferroni test was used for comparison of each pair of variables with a significant difference as a *post hoc* test. *p* values less than 0.05 were considered to be statistically significant. All statistical analyses were conducted using SPSS statistics ver.25 (IBM Corp.).

Ethical consideration

This study was approved by the Research Ethics Committee of Tokushima University Hospital (approval number 2745). We firstly distributed an explanation sheet and a consent form to the manager in the company, and we received written informed consent after explanation regarding the study. After that, we recruited participants through the general affairs division in the company and health care center. The subjects were only men who agreed to participate after explanation by using the explanation sheet through the manager in the company. The explanation sheet included an explanation about the respect for autonomy and anonymization of personal data.

Results

Of the total of 1891 questionnaires that were sent, 1561 were collected (response rate of 82.5%). We excluded 26 participants who were under 20 years of age, 11 participants who were fixed night shift workers and 24 participants for whom ages were not known, and we analyzed data for 1500 rotating night shift workers. As can be seen in Table 1, the

Table 1. Baseline characteristics.

	Number	Proportion (%)
Age (years) (n = 1524)		
20–29	451	29.7
30-39	237	15.6
40-49	382	25.1
50-59	337	22.1
≥60	93	6.1
missing	24	1.6
Duration of shiftwork (years) ($n = 1500$)		
<10	570	38.0
11–19	270	18.0
20–29	319	21.3
30–39	198	13.2
≥40	129	8.6
missing	14	0.9
Types of shift $(n = 1500)$		
three-shift work	1110	74.0
two-shift work	343	22.9
others	46	3.1
missing	1	0.1
Employment status ($n = 1500$)		
regular employee	1301	86.7
contract employee	117	7.8
dispatched employee	31	2.1
part-time workers	7	0.5
others	31	2.1
missing	13	0.9

proportion of rotating night shift workers whose occupational duration was less than 10 years was 38.0%, which was the highest proportion, and 74% of the shift workers worked three shifts. Most of the participants (86.7%) were full-time workers.

We showed the proportion of men who reported any symptoms regardless of degrees in Table 2. There were high proportions in all age groups for the following symptoms: increased need for sleep and often feeling tired, decrease in muscular strength and physical exhaustion/lacking vitality. In men in their 20 s and 30 s, there were high proportions of men with increased need for sleep and often feeling tired and irritability.

The proportions of men with somatic symptoms such as decrease in muscular strength, joint and muscular pain and physical exhaustion/lacking vitality prominently increased with advance of age. The proportion of men with decrease in sexual function also increased with advance of age. On the other hand, the proportion of men with symptoms such as increased need for sleep, often feeling tired, irritability and depressive mood were high in the younger age groups as well as the older age groups.

As can be seen in Figure 1, the median (25–75 percentiles) total AMS score in all of the men was 26 (21–35). The median total AMS scores were 23 in men in their 20 s, 25 in men in their 30 s, 28 in men in their 40 s, 30 in men in their 50 s and 29 in men in their 60 s. There were significant differences in total AMS scores among the age groups (p < 0.001). Significant differences in AMS score were found between men in their 20 s and those in their 40 s or those in their 50 s or those in their 60 s (p < 0.001). There were also significant differences between men in their 30s and those in their 50 s (p = 0.001) and between men in their 30 s and those in their 60 s (p = 0.035). As can be seen in Table 3, the proportions of men with mild, moderate and severe symptoms increased in all ages with advance of age until 60 years.

We categorized the items of AMS into somatic symptoms, psychological symptoms and sexual symptoms, and we compared AMS scores among the age groups (Table 4). There were significant differences in AMS scores for somatic symptoms between men in their 20 s and those in their 40 s or 50 s (p < 0.001), between men in their 30s and those in their 40s (p = 0.002) and between men in their 30 s and those in their 50 s (p < 0.001). We found no significant difference in the AMS scores for psychological symptoms among the age groups. There were significant differences in AMS scores for sexual symptom between men in their 20 s and those in their 30 s, 40 s, 50 s or 60 s (p < 0.001), between men in their 30 s and those in their 40 s or 50 s or 60 s (p < 0.001) and between men in their 40 s and those in their 50 s or 60 s (p < 0.001).

Discussion

The proportions of rotating night shift workers who complained of increased need for sleep and often feeling tired were more than 60% in all age groups. We found that the proportions of men with somatic symptoms such as decrease in muscular strength and joint and muscular pain and the proportions of with sexual symptoms increased with advance of age excluding 60 s. The median AMS scores ranged from 23 to 30, and the score increased with advance of age. Significant differences in AMS scores for somatic symptoms and sexual symptoms were found among the age groups, but a significant difference in the AMS scores for psychological symptoms was not found among the age groups. In 969 men aged 40-80 years in China, somatic and sexual subscores showed significant differences among different age groups [18]. The results of our study for shift workers are consistent with the results of that study.

Symptoms with high frequencies in all workers were increased need for sleep and often feeling tired, suggesting that these symptoms are common male rotating night shift workers. Symptoms with high frequencies in men in their 20s and 30s included

Table 2. Proportion of AMS symptoms according to age.

		Total (<i>n</i> = 1500)		20s (n = 451)		30s (n = 237)		40s (n = 382)		50s (n = 337)		60s (n = 93)	
	Symptoms	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
1	Decline in your feeling of general well-being	761	50.7	171	37.9	118	49.8	211	55.2	208	61.7	53	57.0
2	Joint pain and muscular ache	797	53.1	133	29.5	123	51.9	228	59.7	251	74.5	62	66.7
3	Excessive sweating	256	17.1	61	13.5	38	16.0	74	19.4	69	20.5	14	15.1
4	Sleep problems	806	53.7	218	48.3	127	53.6	219	57.3	197	58.5	45	48.4
5	Increased need for sleep, often feeling tired	974	64.9	278	61.6	151	63.7	262	68.6	227	67.4	56	60.2
6	Irritability	824	54.9	235	52.1	140	59.1	228	59.7	183	54.3	38	40.9
7	Nervousness	603	40.2	167	37.0	97	40.9	167	43.7	144	42.7	28	30.1
8	Anxiety	457	30.5	130	28.8	69	29.1	125	32.7	113	33.5	20	21.5
9	Physical exhaustion / lacking vitality	891	59.4	185	41.0	133	56.1	268	70.2	241	71.5	64	68.8
10	Decrease in muscular strength	911	60.7	173	38.4	144	60.8	261	68.3	263	78.0	70	75.3
11	Depressive mood	661	44.1	175	38.8	105	44.3	180	47.1	161	47.8	40	43.0
12	Feeling that you have passed your peak	532	35.5	58	12.9	69	29.1	154	40.3	194	57.6	57	61.3
13	Feeling burnt out, having hit rock-bottom	315	21.0	62	13.7	41	17.3	98	25.7	91	27.0	23	24.7
14	Decrease in beard growth	178	11.9	14	3.1	22	9.3	62	16.2	64	19.0	16	17.2
15	Decrease in ability/frequency to perform sexually	536	35.7	49	10.9	69	29.1	161	42.1	200	59.3	57	61.3
16	Decrease in the number of morning erections	542	36.1	49	10.9	71	30.0	168	44.0	195	57.9	59	63.4
17	Decrease in sexual desire/libido	368	24.5	40	8.9	44	18.6	109	28.5	138	40.9	37	39.8

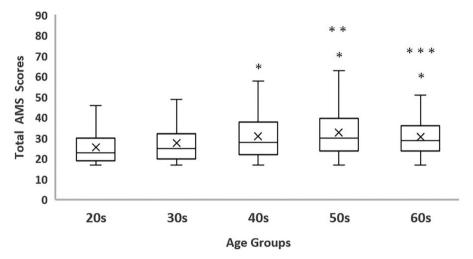


Figure 1. Total AMS scores according to age. The bottom line, middle line and top line of box-and-whisker plot indicate 25 percentile, median, and 75 percentile, respectively. Crosses show the mean values. *20s vs 40s or 50s or 60s (p < 0.001), **30s vs 50s (p = 0.001) ***30s vs 60s (p = 0.035).

Table 3. Degrees of symptoms according to age.

	Degree of symptoms (Total AMS scores)							
Age (years)	No symptoms (17–26)%	Mild (27-36) %	Moderate (37–49) %	Severe (50–85) %				
20–29	69.5	20.1	8.6	1.7				
30-39	58.0	26.9	11.9	3.2				
40-49	46.7	27.8	19.5	5.9				
50-59	37.2	30.9	25.7	6.3				
60–69	39.7	39.7	15.1	5.5				

Values indicate the proportions of subjects.

increased need for sleep, often feeling tired and irritability. The proportion of male respondents who felt that they could not get any rest or could not get sufficient rest from sleeping were 23.2% in men in their 20 s, 27.6% in men in their 30 s, 30.9% in men in their 40 s, 28.4% in men in their 50 s and 15.0% in men in their 60s in the National Health and Nutrition Examination Survey in 2017 in Japan [19]. Night shift workers in their 20 s, 30 s, and 40 s are likely to need more sleep than other ordinary men. The problem of insufficient sleep that was a complaint made by high proportions of the participants in all age groups may be a common problem for rotating night shift workers, whose lifestyle is not in tune with circadian rhythm. Circadian rhythm has been shown to be disturbed in night shift workers [20]. Previous study showed that melatonin level related to circadian rhythm was associated with levels of reproductive hormones including



Table 4. Psychological symptoms, somatic symptoms and sexual symptoms in AMS according to age.

Numbers		20s 385	30s 204	40s 308	50s 258	60s 73	All subjects 1228	Significance
All symptoms	Median 25–75% tile	23 19–30	25 20–32.75	28 22–38	30 24–40	29 23.5–36	26 21–35	20s vs 40s or 50s or 60s (<i>p</i> < 0.001) 30s vs 50s (<i>p</i> = 0.001) 30s vs 60s (<i>p</i> = 0.035)
Psychological symptoms (5 items) 5–25 points	Mean (±SD) Median 25–75% tile Mean (±SD)	25.5(±8.9) 7 5-10 8.0 (±3.7)	27.7 (±10.3) 7 5–9.75 8.1 (±3.7)	30.9 (±11.2) 7 5–11 8.7 (±4.0)	32.9 (±11.2) 7 5–10 8.5 (±3.7)	30.7 (±9.6) 6 5–8.5 7.5 (±3.1)	29.1 (±10.7) 7 5–10 8.3 ± 3.8	ns
Somatic symptoms (7 items) 7–35 points	Median 25–75% tile	10 8–14	11.5 9–15.75	14 10–17	14 11–18.25	13 10.5–16	12 9–17	20s vs 40s or 50s $(p < 0.001)$, 20s vs 60s $(p = 0.002)$, 30s vs 40s $(p = 0.002)$, 30s vs 50s $(p < 0.001)$
Sexual symptoms (5 items) 5–25 points	Mean (±SD) Median 25%–75% tile	11.8 (±4.7) 5 5–5	12.8 (±5.1) 5 5–8	14.3 (±5.2) 7 5–10	15 (±5.1) 9 6–12	13.6 (±4.5) 9 6–12	13.4 ± 5.1 6 5–9	20s vs 30s or 40s or 50s or 60s (p < 0.001), 30s vs 40s or 50s or 60s(p < 0.001),
	Mean (±SD)	5.7 (±3.7)	6.9 (±3.7)	7.9 (±4.0)	9.4 (±3.7)	9.6 (±3.1)	7.5 ± 3.8	40s vs 50s or 60s ($p < 0.001$)

SD: standard deviation.

androgen [21]. Androgen level may be influenced by rotating night shift work [21].

We showed that the proportions of men who had mild, moderate or severe male climacteric symptoms according to AMS scores were 42.0% in men in their 30 s, 53.3% in men in their 40 s and 62.8% in men in their 50 s. The result was similar to the result among men who underwent health examinations in the previous study [6]. Also, we showed that there were significant differences in total AMS scores between men in their 20 s and those in their 40 s or 50 s and between men in their 30 s and those in their 40 s or 50 s. Kobayashi et al.[22] reported that mean total AMS scores were 33.9 in 155 healthy men (mean age, 55.5 years) who received medical checkups and 52.1 in 116 outpatients (mean age, 53.2 years) who complained of male climacteric symptoms at a urology department. Thus, the total AMS score in the present study was similar to that in healthy men in the previous study [22].

The results obtained from AMS scores according to the AMS cluster differed from the results obtained from total AMS score. We showed that the proportions of men with decrease in muscular strength and with joint and muscular pain were high in men in their 50 s and 60 s. The proportions of men in their 30 s with decrease in muscular strength and with joint and muscle pain were 1.6-1.8 times higher than the proportions of men in their 20s, and that proportions gradually increased until 50 s. In addition, there were significant differences in somatic AMS scores between men in their 30 s and those in their 40 s and between men in their 30s and those in their 50s, suggesting that there is a difference in each decade of life in that age range. For somatic symptoms, there were marked differences in the decrease in muscular strength among the age groups. The increase in the proportion of men with decrease in muscular strength may be due to testosterone deficiency with advance of age. Kobayashi et al. [22] reported that the mean somatic AMS scores were 8.4 in men who received medical examinations and 14.8 in men with male climacteric symptoms in men in their 50s in the present study, were similar to the values in men with male climacteric symptoms in that previous study. Rotating night shift workers may have somatic symptoms that are same as those in men with male climacteric symptoms. Testosterone has roles for increasing muscle strength and maintaining sexual function. Decreased testosterone level might be associated with decrease in muscular strength in night shift workers. Recently, sarcopenia in older adults has been focused on as one of the geriatric syndromes, and the importance of bioelectrical impedance analysis for assessment of muscle mass was suggested [23]. Measurement of muscle mass may be needed for rotating night shift workers in a company.

Muscle power of the trunk in rotating night shift workers who are working in the manufacturing industry may be maintained since they stand for long hours and have the same posture in a sitting position, but they may feel a decrease in muscle power in other sites of the body. Asbitt et al. [24] reported that metabolic disturbance in muscles caused by irregular working hours resulted in a decrease in muscle strength.

The proportion of men in the present study who reported sexual symptoms was small, but the proportion increased with advance of age. In addition, there were significant differences in AMS scores for sexual symptoms between men in their 30 s and those in their 40 s and between men in their 40 s and those in their 50 s. Kobayashi et al. [22] reported that mean sexual AMS scores were 12.9 in men who received medical examinations and 15.6 in men with male climacteric symptoms. The mean AMS score for sexual symptom in the present study was 7.5, and this level was lower than that in the previous study [22]. Haider et al. [25] reported that AMS scores decreased in a testosterone-treated group, suggesting that testosterone therapy is effective for improvement of sexual function and quality of life. In addition, Rao et al. [26] reported that treatment with Trigonella foenum-graecum seed extract improved sexual function in middle-aged and older men. Medical treatment should be considered for night shift workers with sexual symptoms.

There were no significant differences among the age groups in psychological symptoms. Notably, there was no significant difference in the mean level of irritability among the age groups. High proportion of men with irritability were found in their 20s and 30s. According to Comprehensive Survey of Living Conditions, the proportions of men who had trouble and stress in daily life were 43.6% in men in their 20 s, 48.0% in men in their 30 s, 48.6% in men in their 40 s, 48.6% in men in their 50 s and 38.5% in men in their 60 s [27]. The results showing that the proportion of men with stress was increased in men in their 20 s and 30 s and that there were high proportions of men in the 40 s and 50 s with stress were similar to the results in general men. We could not clarify whether irritability in men in their 20s and 30s was due to androgen deficiency or due to job-related stress or stress caused by personal life. Trinick et al. [28] suggested that increase in psychological stress related to occupation may be associated with occurrence of LOH syndrome based on the results in a Web survey by using AMS in 10,896 respondents aged 16-89 years in the USA and in England. Kobayashi et al. reported that mean psychological AMS scores were 13.9 in men who received medical checkups and 22.3 in men with male climacteric symptoms [22]. The mean psychological AMS score, which was 8.3 in the present study, was lower than that in men who received medical checkups and men with male climacteric symptoms in the previous study. The fact that a large number of participants did not give an answer regarding the symptom of feeling burnt out or having hit rock-bottom might have affected the AMS score.

It has been suggested that various factors such as change in the social environment and psychological factors are involved in the occurrence of male climacteric symptoms [29]. Also, it has been reported that visiting a hospital at an early stage of symptoms and appropriate treatment can improve quality of life [30]. Since the publication of a clinical practice manual for LOH syndrome by the Japanese Urological Association in 2007 [31], male climacteric symptoms have been recognized among medical workers. However, unlike the recognition of female climacteric symptoms, the recognition of male climacteric symptoms in the general population is still poor. Therefore, sufficient efforts are not made to visit a hospital or improve lifestyle habits. It has been reported that the proportion of men who complain of male climacteric symptoms has been increasing with increasing recognition of LOH symptoms and male climacteric symptoms [32]. Medical examinations and educational activities in the workplace are needed since most young to middleaged men are working.

Since night shift work has harsh working conditions that disturb circadian rhythm, LOH syndrome might occur more frequently in young rotating night shift workers than in young daytime workers. An organization strategy of mental health for rotating night shift workers is needed to prevent LOH syndrome and detect LOH syndrome at an early stage. It has been reported that the degree of awareness of andropause in men over 40 years of age was very low, though they had experienced symptoms of andropause [4]. Occupational health nurses should make a proposal to include an AMS questionnaire in medical checkups and they should recommend employees who have a high AMS score to visit a hospital. Moreover, occupational physicians and occupational health nurses

should play important roles for providing information regarding male climacteric symptoms and education for employees regarding knowledge of LOH at a safety and health committee. However, since many small- to medium-sized companies in Japan do not have occupational physicians and nurses, cooperation with health officers and health insurance societies may be necessary. It has been reported that symptoms will get worse if men with LOH syndrome do not receive appropriate treatment [29]. If shift workers recognize their symptoms as male climacteric symptoms and visit a hospital, a beneficial economic effect can be expected due to a reduction in absenteeism and increase in productivity through somatic and psychological health promotion. Assessment by using AMS scores is widely used in various countries as screening for LOH syndrome. Measurement of free testosterone level is necessary for men with high AMS scores [33,34].

The strength of this study is the large sample size. There was no previous study with a sample size as large as that in our study. Previous studies have been conducted using the AMS scale for daytime workers but not for rotating night shift workers. However, this study also has several limitations. First, a causal relationship was not clarified since this study was a crosssectional design. Secondly, no significant difference was observed between men in their 50s and those in their 60s since the number of men in their 60s was small and the age of men in their 60 s was less than 63 years. The results of our study might be different from the results for men in their 60 s in a previous study [6]. Also, the number of men who do not answer questions regarding sexual symptoms is much that might influence the AMS score. Further study may be needed with large numbers of men in their 50 s and 60 s, who are more likely to have male climacteric symptoms. The generalizability of the obtained results is inconclusive for all shift workers since there are various types of shift work. Questionnaires regarding LOH syndrome have been developed in various countries and their validity and reliability have been examined [33,35-37]. Horie et al. [38] also reported that sexual perceptions were different in Japanese and Caucasian populations. An appropriate questionnaire for each country should be considered.

In conclusion, we found significant age-dependent differences in somatic symptoms and sexual symptoms in rotating night shift workers. More than 60% of the participants reported increased need for sleep and often feeling tired in all age groups. The

prevalence of somatic symptoms and sexual symptoms remarkably increased with advance of age. However, the prevalence of psychological symptoms was high in the younger age groups as well as older age groups.

Acknowledgements

The authors would like to show our greatest appreciation to participants, managers of general affairs and occupational nurses. We are also grateful for assistance given by Professor Iwamoto.

Disclosure statement

The authors declare there is no conflicts of interest.

Funding

This study was supported in part by grants-aid for Shikoku University research grant.

Notes on contributors

Sachiko Kubo joined Shikoku-University as an Assistant Professor in 2014. She obtained her master's degree of Nursing Science from Tokushima University Graduate School of Health Sciences in 2013. Her research field is occupational health and adult nursing.

Toshiyuki Yasui is M.D., Ph.D., Professor of Reproductive and Menopause Medicine of Reproductive and Menopause Medicine. In 2019, He was appointed as a dean of Tokushima University Graduate school of Health Sciences. He received his doctorate in Medicine from Tokushima University 1991. His recent research paper includes Different levels of awareness and knowledge of male climacteric in female nurses and female office workers (2015), Associations of endogenous sex hormones and sex hormone-binding globulin with lipid profiles in aged Japanese men and women (2008), Androgen in postmenopausal women (2012). His research field is endocrinology in aging, role of androgen in female, bone and lipid metabolism in postmenopausal medicine, reproductive endocrinology.

Masahito Tomotake is M.D., Ph.D., Professor of Mental Health at Tokushima University Graduate school of Health Sciences. In 2019. His recent treatise includes Clinical factors influencing resilience in patients with anorexia nervosa (2018), Relationship between social and cognitive functions in people with schizophrenia (2018). He obtained his doctorate in Medicine from Tokushima University in 1997. His field of study is Etiology of mental disorders, evaluation of mental disorders, prevention against mental disorders.

Yukie Matsuura is an Assistant Professor of Health Science at the Tokushima University. She received her master degree in nursing science from Japanese Red Cross College of Nursing

(2008). Her research interests cover wide areas of nursing and health care including maternal and child health, adolescent health, menopausal health, elderly health care etc. Her current research is doing on premenstrual symptoms among young females.

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