J. Phys. Ther. Sci. 29: 1129–1133, 2017

The Journal of Physical Therapy Science

Original Article

Relationship of locomotive syndrome with health-related quality of life among patients with obstructive sleep apnea syndrome

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Abstract. [Purpose] This study aimed to examine the prevalence of locomotive syndrome among patients with obstructive sleep apnea syndrome (OSAS) using the "loco-check" recently developed by the Japanese Orthopedic Association, and to compare health-related quality of life (HRQOL) among patients with and without locomotive syndrome. [Subjects and Methods] This cross-sectional study evaluated 1,195 outpatients with OSAS (1,030 males and 165 females). Locomotive syndrome was evaluated using the Japanese Orthopedic Association's "loco-check". HRQOL and psychological distress were evaluated using the EuroQol 5-dimensional (EQ-5D) and 6-item Kessler questionnaires. [Results] Locomotive syndrome was detected in 578 patients (48.4%), including 398 males (38.6% of males) and 119 females (70.3% of females). Patients with OSAS and locomotive syndrome had significantly lower EQ-5D scores, compared to patients without locomotive syndrome. Multiple regression analysis revealed that HRQOL among patients with OSAS was independently associated with locomotive syndrome, age, gender, body mass index, apnea hypopnea index, the Japanese version of the Epworth Sleepiness Scale score, and exercise habits. [Conclusion] The prevalence of locomotive syndrome was thought to be comparatively high in patients with OSAS, and locomotive syndrome was associated with lower HRQOL, even after adjusting for confounding factors. Prevention or management of locomotive syndrome may be beneficial for improving HRQOL among patients with OSAS.
Key words: Obstructive sleep apnea syndrome (OSAS), Locomotive syndrome, Health-related quality of life (HRQOL)

(This article was submitted Mar. 7, 2017, and was accepted Apr. 5, 2017)

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is closely linked to traffic and occupational accidents that are caused by daytime somnolence, and has become a public health challenge in Japan. Chronic apnea-induced hypoxia causes activation of the sympathetic nerves, oxidative stress, inflammation, and vascular endothelial disorders, which are associated with increased prevalences of hypertension and cerebro-cardiovascular diseases[1, 2)], as well as a higher mortality rate[3–5)]. Therefore, effective preventative and therapeutic interventions are urgently needed for OSAS. Some reports have described an association between OSAS and obesity, with approximately 50% of obese males and 8–38% of obese females having OSAS[6, 7)]. The Japanese Respiratory Society has reported that 3–7% of adult Japanese males and 2–5% of adult Japanese females have OSAS[8)].

Continuous positive airway pressure (CPAP) therapy is commonly used for patients with OSAS. However, CPAP therapy cannot improve obesity of the major problem, and weight loss by exercise therapy is one of direct treatments. We have previ-

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ously reported that patients with OSAS have significantly less lower leg muscle mass, compared to patients without OSAS[9], and lower leg strength is a risk factor for falls[10]. These findings might suggest that patients with OSAS have locomotive dysfunction, which would indicate that their reduced lower leg muscle mass and strength must be considered when designing exercise therapy. However, the small sample size and complicated measurements of muscle mass and strength make it difficult to account for this relationship in clinical practice.

The Japanese Orthopedic Association (JOA) recently developed a questionnaire regarding locomotive dysfunction (the "loco-check")[11]. This questionnaire allows researchers to quickly and easily evaluate locomotive dysfunction, and the results may be useful for implementing appropriate exercise therapy. Moreover, there is a close relationship between locomotive syndrome and health-related quality of life (HRQOL) among community-dwelling Japanese people[12], although no studies have evaluated the relationship between locomotive syndrome and HRQOL among patients with OSAS. Therefore, the present study evaluated the prevalence of locomotive syndrome among Japanese patients with OSAS, as well as the association between HRQOL and locomotive syndrome.

SUBJECTS AND METHODS

This cross-sectional study evaluated 1,195 outpatients (1,030 males and 165 females) with OSAS who were treated using CPAP at the KKR Takamatsu Hospital (Kagawa, Japan) during November–December 2016. Patients were excluded if they had acute or chronic musculoskeletal disorders, other sever neurological or endocrine disorders, or a history of stroke. All included patients provided their written informed consent, and the study's protocol was approved by the research ethics committee of KKR Takamatsu Hospital (E111) and conformed to the tenets of the Declaration of Helsinki.

Standard methods were used to collect data regarding gender, age, height, body weight, body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP). The patients' clinical records were also evaluated to determine the duration of their OSAS and their apnea hypopnea index (AHI). The severity of OSAS was calculated on the basis of the patient's AHI (number of apneas and hypopneas per hour), and classified into three categories: mild (5–15/h accompanied by typical clinical symptoms), moderate (16–29/h), and severe (≥30/h)[13]. Well-trained medical staff interviewed each patient to determine their score for the Japanese version of the Epworth Sleepiness Scale (JESS)[14] and their exercise habits (aerobic exercise [e.g., walking or jogging] for >30 min three times per week during a 6-month period). The JESS questionnaire examines daytime somnolence and consists of eight questions regarding daily activities. Participants were asked to assess their likelihood of dozing off or falling asleep in certain situations, and the responses were scored as 0 points (no chance of dozing off), 1 point (a slight chance of dozing off), 2 points (a moderate chance of dozing off), or 3 points (a high chance of dozing off). Total scores of >10 indicate excessive daytime somnolence.

The JOA's "loco-check" for locomotive syndrome, which was simply and conveniently applicable, was developed in 2007[11], and identifies a participant as possibly having locomotive syndrome if they agree with at least one of seven statements. The seven statements are (1) you cannot put on a pair of socks while standing on one leg, (2) you stumble or slip in your home, (3) you need to use a handrail when going upstairs, (4) you cannot cross the road at a crossing before the traffic light changes, (5) you have difficulty walking continuously for 15 min, (6) you find it difficult to walk home carrying a shopping bag that weighs approximately 2 kg (e.g., two 1-L milk cartons), and (7) you find it difficult to complete housework that requires physical strength (e.g., use of a vacuum cleaner or moving futons in and out of a closet).

HRQOL was evaluated using the EuroQol 5-dimensional (EQ-5D) questionnaire[15], which generates assessment scores for five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses in each dimension are divided into three categories: no problems, moderate problems, or extreme problems. The EQ-5D health state is defined by combining one level from each of the five dimensions, and produces a set of utility values as previously described[16].

Psychological distress was evaluated using the 6-item Kessler scale (K6), which is widely used to screen for psychological distress in the general population[17, 18]. The K6 tool is a self-administered questionnaire that consists of six questions to evaluate depressive moods and anxiety during the preceding 4 weeks using a 5-point scale (scores of 0–4). The total score is the equally weighted sum of the scores for the six items, with possible scores ranging from 0 to 24. We classified patients who had a score of >13 points as being in a depressive state[18].

Data were expressed as mean ± standard deviation. The unpaired t-test and χ^2 test were used to compare the clinical parameters between patients with OSAS and with and without locomotive syndrome. Analysis of covariance was used to adjust for confounding factors, which were defined as factors with a univariate p-value of <0.05. Multiple regression analysis was used to evaluate the association of HRQOL with locomotive syndrome among patients with OSAS. All data were analyzed using JMP software (version 12.1.0; SAS Institute, Cary, NC, USA).

RESULTS

The clinical characteristics of the patients with OSAS are summarized in Table 1. The study included 1,030 males and 165 females. The group included 578 patients with locomotive syndrome (48.4%), including 398 males (38.6% of males) and 119 females (70.3% of females). The mean EQ-5D score was 0.891 ± 0.178.

Table 1. Clinical characteristics of the patients with obstructive sleep apnea syndrome

	Total (1,195)	Males (1,030)	Females (165)
Age (years)	61.3 ± 12.9	60.6 ± 12.8	65.3 ± 13.0
Height (cm)	165.5 ± 8.3	167.6 ± 6.4	152.2 ± 6.7
Body weight (kg)	75.9 ± 15.1	77.7 ± 14.2	65.2 ± 16.4
BMI (kg/m^2)	27.7 ± 4.7	27.6 ± 4.5	28.0 ± 6.0
SBP (mmHg)	134.2 ± 11.7	134.4 ± 11.7	132.8 ± 11.8
DBP (mmHg)	75.9 ± 10.1	76.2 ± 10.1	73.9 ± 9.8
Duration of OSAS (months)	69.8 ± 50.0	72.1 ± 50.7	55.7 ± 42.9
AHI	2.83 ± 3.36	2.83 ± 3.18	2.82 ± 4.33
JESS	5.81 ± 4.41	5.84 ± 4.38	5.64 ± 4.62
EQ-5D score	0.891 ± 0.178	0.903 ± 0.174	0.815 ± 0.182
K6 score	1.72 ± 2.88	1.62 ± 2.81	2.35 ± 3.20
Locomotive syndrome (n/%)	578 (48.4)	459 (44.6)	119 (70.3)
Exercise habits (n/%)	453 (37.9)	391 (40.0)	62 (37.6)
Complication			
Hypertension (n/%)	455 (38.1)	398 (38.6)	57 (34.6)
Type 2 diabetes (n/%)	317 (26.5)	275 (26.7)	42 (25.5)
Hyperlipemia (n/%)	255 (21.3)	223 (21.7)	32 (19.4)
Cardiovascular disease (n/%)	200 (16.7)	177 (17.2)	23 (13.9)

Values are presented as mean ± SD.
BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; OSAS: obstructive sleep apnea syndrome; AHI: apnea hypopnea index; JESS: Japanese version of the Epworth Sleepiness Scale; EQ-5D: EuroQol 5-dimensional questionnaire for evaluation of health-related QOL.
K6 score for evaluating psychological distress.

Table 2. Comparing the clinical parameters of patients with and without locomotive syndrome

	Locomotive syndrome (+)	Locomotive syndrome (–)	p	p^1	p^2
Subjects (n/%)	578 (48.4)	617 (51.6)			
Age (years)	65.9 ± 12.2	56.9 ± 12.0	**		
Height (cm)	163.4 ± 9.2	167.3 ± 7.0	**		
Body weight (kg)	75.2 ± 16.6	76.6 ± 13.6		**	
BMI (kg/m^2)	28.0 ± 5.1	27.3 ± 4.2	**	**	
SBP (mmHg)	133.9 ± 12.1	134.5 ± 11.3			
DBP (mmHg)	73.4 ± 10.2	78.0 ± 9.4	**	**	**
Duration of OSAS (months)	73.4 ± 50.5	66.5 ± 49.3	*		
AHI	3.12 ± 4.05	2.56 ± 2.51	**		
JESS	5.94 ± 4.53	5.69 ± 4.30		**	
EQ-5D score	0.834 ± 0.211	0.944 ± 0.116	**	**	**
K6 score	2.14 ± 3.20	1.33 ± 2.46	**	**	**
Exercise habits (n/%)	205 (35.5)	248 (40.2)			
Complication					
Hypertension (n/%)	265 (45.9)	190 (30.8)	**		
Type 2 diabetes (n/%)	193 (33.4)	124 (20.1)	**		
Hyperlipemia (n/%)	138 (23.9)	117 (19.0)	*		
Cardiovascular disease (n/%)	133 (23.0)	67 (10.9)	**		

Values are presented as mean ± SD. *p<0.05, **p<0.01
P1: Adjusting for age and gender; P2: Adjusting for age, gender, BMI, duration of OSAS, AHI, JESS; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; OSAS: obstructive sleep apnea syndrome; AHI: apnea hypopnea index; JESS: Japanese version of the Epworth Sleepiness Scale; EQ-5D: EuroQol 5-dimensional questionnaire for evaluation of health-related QOL.
K6 score for evaluating psychological distress.

Table 2 shows the clinical characteristics of patients with and without locomotive syndrome. Compared to patients without locomotive syndrome, patients with OSAS and locomotive syndrome had significantly higher values for age, BMI, duration of OSAS, AHI, K6 score, hypertension, type 2 diabetes, hyperlipidemia, and cardiovascular disease. However, patients with OSAS and locomotive syndrome had lower values for height, DBP, and EQ-5D score. After adjusting for age and gender, patients with OSAS and locomotive syndrome had significantly higher values for BMI, JESS score, and K6 score, but significantly lower values for body weight, DBP, and EQ-5D scores. After adjusting for age, gender, BMI, duration of OSAS, AHI, and JESS score, patients with OSAS and locomotive syndrome had significantly higher K6 scores and significantly lower values for DBP and EQ-5D score.

Table 3. Multiple regression analyses of EQ-5D scores and clinical parameters

	B	β	95% CI		p
Constant	1.10850	0	1.00562	1.21138	**
Locomotive syndrome	–0.03927	–0.2212	–0.04981	–0.02873	**
JESS	–0.00555	–0.13793	–0.00775	–0.00335	**
Age	–0.00189	–0.13714	–0.00281	–0.00096	**
Gender	–0.02887	–0.11226	–0.04287	–0.01487	**
BMI	–0.00280	–0.07407	–0.00505	–0.00055	*
AHI	–0.00344	–0.06502	0.00628	–0.00061	*
Exercise habits	0.01508	0.08244	0.00510	0.02506	**
Duration of OSAS	–0.00001	–0.00282	–0.000201	0.00018	

R^2=0.14, analysis of covariance p=0.0001.
B: partial regression coefficient; β: standardized partial regression coefficient; BMI: body mass index, OSAS: obstructive sleep apnea syndrome; AHI: apnea hypopnea index, JESS: Japanese version of the Epworth Sleepiness Scale; EQ-5D: EuroQol 5-dimensional questionnaire for evaluation of health-related QOL

Multiple regression analysis was used to evaluated the 1,195 patients with OSAS using EQ-5D score as the dependent variable and defining the independent variables as age, gender, BMI, AHI, duration of OSAS, JESS score, and locomotive syndrome. Among patients with OSAS, EQ-5D was independently associated with locomotive syndrome, JESS score, age, gender, BMI, and AHI (Table 3). Among these factors, locomotive syndrome was most strongly associated with lower EQ-5D scores.

DISCUSSION

Our main objective in this cross-sectional study was to examine the prevalence of locomotive syndrome among patients with OSAS, and to compare HRQOL among patients with and without locomotive syndrome. The prevalence of locomotive syndrome was 48.4% among patients with OSAS in the present study. A slightly lower prevalence was reported by Iizuka et al., who found that the prevalence of locomotive syndrome was 39.6% among 442 community-dwelling people[12]. Both studies' groups had similar ages, although the patients in the present study had a higher mean BMI (28.0 ± 5.1kg/m^2 vs. 24.0 ± 3.5 kg/m^2)[12]. In this context, obesity is known to be closely associated with locomotive syndrome[19], and the prevalence of locomotive syndrome among patients with OSAS is higher than that among community-dwelling people. In the present study, we found that locomotive syndrome was most common among females with OSAS, compared to males (70.3% vs. 44.6%). Sasai et al. have also reported that the prevalence of locomotive syndrome was higher among females, compared to males (35.6% vs. 21.2%)[20]. The decrease in bone density and physical activity after menopause may explain the higher prevalence of locomotive syndrome among females[19]. Moreover, the prevalence of locomotive syndrome among patients with OSAS patients was approximately two-fold higher, compared to the prevalence among community-dwelling people. Thus, OSAS and obesity may contribute to the development of locomotive syndrome.

HRQOL among patients with OSAS and locomotive syndrome was significantly lower, compared to patients without locomotive syndrome, even after adjusting for age, gender, BMI, duration of OSAS, AHI, and JESS score. Furthermore, the multiple regression analysis revealed that the presence of locomotive syndrome (as evaluated using the "loco-check") was the strongest determinant of HRQOL (β=−0.22, p<0.01). Thus, our findings suggest that locomotive syndrome among patients with OSAS was closely associated with reduced HRQOL. In this context, the "loco-check" comprehensively evaluates locomotive function based on muscle strength, balance, exercise tolerance, and walking ability, and these findings can be used to reduce the patient's body weight when treating cases of OSAS. Peppard et al. reported that a 10% reduction in body weight was associated with a 26% reduction in AHI, and that a 10-kg reduction in body weight was associated with clinical improvements among patients with moderate-to-severe OSAS[21]. Furthermore, the American College of Physicians strongly recommends treating obesity among patients with OSAS[22]. The present study's multiple regression analysis also revealed that exercise habits and locomotive syndrome were associated with HRQOL. Moreover, Kawahara et al. have reported that CPAP therapy improved HRQOL among patients with OSAS[23]. Therefore, it appears that patients with OSAS may experience a clinical benefit from exercise education and continuous CPAP therapy.

The present study has several limitations. The first limitation is the cross-sectional design, which is limits our ability to comment on the causality of the associations that were observed. Second, all patients with OSAS were being treated using CPAP and their clinical status was relatively well controlled, which limit the generalizability of our findings to all patients with OSAS. Although further studies are needed to validate our findings, it appears that exercise education might be beneficial for improving HRQOL among patients with OSAS.

In conclusion, the present cross-sectional study revealed that the prevalence of locomotive syndrome was relatively high among patients with OSAS, and that low HRQOL was associated with locomotive syndrome among patients with OSAS.

Conflicts of interest

The authors have no financial or personal relationships that could pose a conflict of interest.

ACKNOWLEDGEMENT

This research was supported in part by research grants from Nankaiikueikai (Kagawa, Japan).

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