Effects of sleep position on the treatment response of oral appliance for obstructive sleep apnea

Ryoichi Akahoshi DDS^a, Souichi Yanamoto DDS, PhD^{a,b}, Yuki Sakamoto DDS, PhD^{a,c}, Tomofumi Naruse DDS, PhD^a, Saki Hayashida DDS PhD^a, Sakiko Soutome DDS PhD^b, Masahiro Umeda DDS, PhD^a

^aDepartment of Clinical Oral Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; ^bOral Management Center, Nagasaki University Hospital, Nagasaki, Japan; ^cDepartment of Oral Surgery, Hironokogen Hospital, Kobe, Japan

Corresponding author:

Souichi Yanamoto

E-mail: syana@nagasaki-u.ac.jp

Department of Clinical Oral Oncology, Unit of Translational Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

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Abstract

Objectives: The influence of sleep position on the efficacy of oral appliance (OA) therapy and the clinical significance of this have not been adequately explained. Hence, this retrospective study aimed to clarify the characteristics of positional obstructive sleep apnea (P-OSA) patients and to examine the relationship between sleep position and the efficacy of OA therapy.

Materials and Methods: Seventy-three patients who underwent polysomnography before and after OA therapy were divided into positional OSA (P-OSA) and non-positional OSA (NP-OSA) groups and examined.

Results: Forty-seven patients had P-OSA, and 26 had NP-OSA. P-OSA was characterized by a relatively high ratio of supine to lateral apnea hypopnea index (AHI), since the lateral AHI of P-OSA was significantly lower than that of NP-OSA. OA therapy was more effective for P-OSA than for NP-OSA. Younger age and the presence of P-OSA are useful as predictors of OA therapy efficacy.

Conclusions: Even for relatively severe OSA, in the case of younger age and/or P-OSA, the application of simple, cost-effective OA therapy may be recommended over other treatment modalities.

Clinical Relevance: The indications for oral appliance therapy consider only the severity of OSA, and our study suggests that even for relatively severe OSA, in the case of younger age and/or positional OSA, the application of a simpler, cost-effective oral appliance therapy might be possible.

1 **Keywords**

2 Obstructive sleep apnea; oral appliance; sleep position; positional obstructive sleep apnea

1 **Introduction**

2 Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder
3 characterized by repetitive upper airway collapse or apnea-hypopnea cycles with sleep
4 fragmentation and intermittent hypoxia. Patients with undiagnosed or untreated OSA
5 have an increased risk of cardiovascular and cerebrovascular events and decreased quality
6 of life [1,2].

7 At present, nasal continuous positive airway pressure (nCPAP) and oral appliance
8 (OA) therapy are widely used in OSA treatment [3,4]. OA therapy is a non-invasive and
9 well-compliant treatment compared to nCPAP, but its treatment effect is inferior. Recently,
10 OA therapy has been reported to not only improve apnea and hypopnea, but also to reduce
11 the risk of complications such as hypertension, arrhythmias, ischemic heart disease, and
12 cerebrovascular disease [5]. The guidelines issued by the American Academy of Sleep
13 Medicine recommended OA therapy for mild to moderate OSA or nCPAP interrupted
14 cases [6]. However, OA therapy has been reported to be effective even in severe OSA [7].
15 Therefore, indication for OA treatment should not be determined based solely on the
16 severity of OSA. To determine the indication for OA therapy, it is important to predict the
17 effect of OA therapy. Some studies have reported on prediction of the treatment effect of
18 OA therapy using cephalometric analysis [8], computed tomography [9], or drug-induced
19 sleep endoscopy [10].

20 Recently, it has been reported that sleep position is associated with OA therapy
21 response [11,12]. In general, OSA leads to more apnea hypopnea events in the supine
22 position than in the lateral position. Positional OSA (P-OSA) is OSA with a positional
23 dependency; patients with P-OSA have a supine apnea hypopnea index (AHI) at least 2
24 times greater than their lateral AHI, and patients with non-positional OSA (NP-OSA)

1 have a supine AHI less than 2 times greater than their lateral AHI [13]. Previous studies
2 have reported that OA therapy is more efficacious in patients with P-OSA [11,12,14].
3 Meanwhile, other studies could not reveal differences in response rates between P-OSA
4 and NP-OSA patients [15,16]. The influence of sleep position on the efficacy of OA
5 therapy and the clinical significance of this have not yet been adequately explained.

6 The purpose of this retrospective study was to clarify the characteristics of patients
7 with P-OSA and to examine the relationship between sleep position and the efficacy of
8 OA therapy.

11 **Materials and methods**

12 ***Patients***

13 This retrospective cohort study included patients with OSA who underwent OA therapy
14 in the Department of Oral and Maxillofacial Surgery at Nagasaki University Hospital
15 between April 2016 and March 2019. OSA was confirmed if the overnight
16 polysomnography (PSG) study showed a documented AHI > 5 respiratory events per hour.
17 Patients who did not undergo PSG with OA were excluded. After excluding patients with
18 inadequate or missing information, the remaining 73 patients were eligible for inclusion.

19 Patients were divided into 2 groups, P-OSA or NP-OSA, according to the criteria used
20 by Cartwright et al. [13]. P-OSA was defined when the supine AHI was at least 2 times
21 greater than the lateral AHI, and the remaining patients were defined as having NP-OSA.
22 In addition, rapid eye movement (REM) predominant OSA was defined by a > 0 REM
23 predominance index (RPI), which was determined using log transformation [$RPI = \log$
24 $(\text{REM AHI} + 0.5) - \log(\text{non-REM AHI} + 0.5)$] [17].

1 This study conformed to the tenets of the Declaration of Helsinki. Ethical approval
2 was obtained from the Institutional Review Board of Nagasaki University (reference
3 number 19081916). Because of the retrospective nature of this study, the requirement for
4 informed consent was waived.

6 ***Oral appliance therapy***

7 The OA comprised two lateral connectors and individual customized appliances for the
8 maxilla and the mandible, as previously reported [8,18]. The appliances were made of
9 clear transparent polyethylene terephthalate glycol thermoplastic (DURAN, Scheu-dental
10 GmbH, Iserlohn, Germany), and the degree of mandibular advancement was set at slightly
11 less than the maximum anterior position so as not to exceed the limit the patients could
12 comfortably tolerate. The position was in fact determined at 70-80% of the maximum
13 protrusion. The portions of the appliance were joined using a connector composed of a
14 polyethylene toothed belt (NK connector, Morita Co. Ltd, Osaka, Japan). If the patient
15 complained of any discomfort in the temporomandibular joints or muscles, the maxillary
16 and mandibular portions were separated and joined again in a less-protruded position. The
17 patients underwent a second PSG to evaluate the efficacy of OA therapy. A successful
18 treatment response was defined as a reduction in AHI with OA $\geq$ 50% compared to
19 baseline and a decrease in AHI to $<$ 10 respiratory events per hour with OA.

21 ***Statistical analysis***

22 Data analysis was performed using the SPSS version 24.0 software (Japan IBM Co.,
23 Tokyo, Japan). Comparison of categorical variables was carried out using Chi-squared or
24 Fisher's exact test, as appropriate. Continuous data between groups were compared with

a non-parametric Mann-Whitney U test or Wilcoxon signed-rank test. Multivariate analysis using logistic regression was performed to evaluate the associations between the predictive variables and the response to OA therapy. In all analyses, 2-tailed P values of < 0.05 were considered statistically significant.

Results

Patients characteristics

Patients characteristics and sleep data are summarized in Table 1. The average patient age was 57.4 years, and 51 male and 22 female patients were included in this study. The mean body mass index (BMI) was 24.3 kg/m². Of the 73 OSA patients, 47 patients had P-OSA, and 26 patients had NP-OSA. Study subjects with P-OSA were significantly older and less obese than those with NP-OSA. There were no statistically significant differences in total AHI, supine AHI, and non-REM AHI between the P-OSA and NP-OSA groups. Lateral AHI and REM AHI occurred significantly less often in the P-OSA group. In addition, REM predominant OSA was significantly more common in the NP-OSA group.

Changes in AHI from baseline to after OA therapy

The median (interquartile range) of total AHI decreased from 16.1 (11.5-20.2) to 6.5 (3.5-8.6) in the P-OSA group ($P<0.001$) and from 17.2 (13.2-24.9) to 8.8 (4.7-13.0) in the NP-OSA group ($P<0.001$) (Figure, a). The median of supine AHI decreased from 23.6 (17.0-34.7) to 7.8 (5.2-12.9) in the P-OSA group ($P<0.001$) and from 19.9 (15.3-4.4) to 12.0 (7.9-18.1) in the NP-OSA group ($P<0.001$) (Figure, b). The median of lateral AHI decreased from 3.7 (0.6-9.0) to 1.0 (0-3.6) in the P-OSA group ($P=0.015$) and from 33.7

(18.6-56.6) to 5.9 (3.7-14.4) in the NP-OSA group ($P<0.001$) (Figure, c). The median of REM AHI decreased from 23.1 (11.2-37.1) to 11.1 (6.3-18.9) in the P-OSA group ($P<0.001$) and from 33.4 (22.7-49.5) to 16.8 (9.1-26.9) in the NP-OSA group ($P<0.001$) (Figure, d). The median of non-REM AHI decreased from 12.6 (8.9-17.7) to 3.6 (2.5-7.7) in the P-OSA group ($P<0.001$) and from 14.8 (7.7-24.3) to 6.3 (1.5-10.5) in the NP-OSA group ($P<0.001$) (Figure, e). OA therapy was effective in reducing the AHI in both P-OSA and NP-OSA patients.

Prediction of successful treatment response of OA therapy

The OA therapy was successful in 55 (75.3%) of the 73 patients. Although the successful treatment response rates tended to be different between patients with P-OSA (83.0%) and NP-OSA (61.5%), this difference was not statistically significant ($P=0.052$). Multivariate analysis using logistic regression showed that age ≥ 58 years (OR=0.213; 95% CI=0.050-0.902; $P=0.036$) and P-OSA (OR=6.544; 95% CI=1.479-28.950; $P=0.013$) were independent predictors of successful treatment response of OA therapy (Table 2).

Discussion

The use of OA therapy for OSA treatment has recently increased. Although OA therapy is generally regarded as less effective compared to nCPAP, there are cases in which the efficacy of OA therapy is often equivalent to that of nCPAP, and OA therapy is known to be cost-effective. Predicting the efficacy of OA therapy is necessary to determine the optimal treatment for patients. We previously reported that the prediction of OA efficacy by cephalometric analysis may be useful to strengthen a patient's motivation for

undergoing nCPAP and to improve adherence to nCPAP, if the OA efficacy is predicted to be low and it is better to shift to nCPAP treatment [8]. Some studies have suggested that the efficacy of OA therapy may be influenced by sleep position [11,12,14-16]. With these considerations, the current study was performed to clarify the characteristics of patients with P-OSA and to examine the relationship between sleep position and the efficacy of OA therapy.

Previous studies reported that approximately 50% to 60% of patients with OSA were diagnosed with P-OSA according to Cartwright's criteria [11,12,19]. In Asian populations, the prevalence has been reported to be higher at 67% [20]. Similarly, the present study of an Asian population indicated that 47 of 73 patients (64.4%) were diagnosed with P-OSA. Teeraprairuk et al. [20] reported that the high prevalence of P-OSA in Asian populations was due to the association between non-obesity and P-OSA, since most Asian populations with OSA are relatively less obese compared to Western populations with more frequently observed craniofacial structural abnormalities. Our results were similar to those obtained by Teeraprairuk et al., revealing that patients with P-OSA had a significantly lower BMI than do those with NP-OSA. In addition, Oksenberg et al. [21] reported that patients with NP-OSA who converted to P-OSA showed a decrease in body weight and improvement of OSA, whereas those with P-OSA who converted to NP-OSA showed an increase in body weight and worsening of OSA. Our results supported this study, also suggesting that those with P-OSA had lower BMIs and mild OSA, but there was no statistically significant difference compared to the NP-OSA group.

In our study, various characteristics of the PSG data from the P-OSA group are interesting. There was no significant difference in supine AHI between the P-OSA and NP-OSA groups. However, participants with P-OSA were characterized by a relatively

high ratio of supine to lateral AHI, because the lateral AHI was significantly lower in the P-OSA group. Furthermore, both REM AHI and REM predominant OSA were significantly higher in the NP-OSA group. Thus, these data suggest that P-OSA is characterized by lower REM AHI than that of NP-OSA.

OA therapy was effective in reducing the AHI in both P-OSA and NP-OSA patients. Some studies reported that supine AHI and lateral AHI were significantly reduced in patients with P-OSA and NP-OSA [12,15]. Furthermore, Dieltjens et al. [15] reported that REM AHI and non-REM AHI were significantly decreased. On the other hand, Sutherland et al. [4] reported that the response rate of OA therapy was low in REM-predominant OSA. However, in our study, in addition to supine AHI and lateral AHI, REM AHI and non-REM AHI were significantly reduced by OA therapy. When successful therapeutic response was defined as a decrease in AHI at > 50% OA and a decrease in AHI to < 10 respiratory events per hour at OA compared to baseline, the success rate was 83.0% in P-OSA and 61.5% in NP-OSA. These results indicate that OA therapy is more effective for P-OSA compared to NP-OSA, as suggested in previous reports [11,12,14].

Our results of multivariate logistic regression analysis revealed that age and the presence of P-OSA are useful as predictors of OA therapy efficacy. A large cohort study [4] identified that younger age (<58 years) and lower obesity were independent predictors of OA therapy response, and Marklund et al. [19] indicated that the odds ratio for OA therapy success was 6.0 in P-OSA patients according to a logistic regression model. Our study also demonstrated that P-OSA was the strongest independent predictor (odds ratio, 6.544; $P=0.013$) of OA therapy success.

This study is limited by its retrospective nature and its bias in case selection by

1 physicians. Indications for OA therapy were applied not only to mild to moderate OSA
2 but also to patients with poor CPAP adherence. The clinical decisions might also have
3 been influenced by biases such as physician choice and OSA severity. Although this study
4 could reveal predictors of OA therapy, the existence of unknown biases, in addition to the
5 use of retrospective data, remains a major limitation.

6 In conclusion, the results of this study indicated that the prevalence of P-OSA was
7 relatively high (64.4%). P-OSA was characterized by a relatively high ratio of supine to
8 lateral AHI because lateral AHI was significantly lower in the P-OSA group than in the
9 NP-OSA group. We determined that OA therapy is more effective for P-OSA compared
10 to NP-OSA. Younger age and the presence of P-OSA are useful as predictors of OA
11 therapy efficacy. Therefore, even for relatively severe OSA, in the case of P-OSA, the
12 application of OA therapy, which is simpler and more cost-effective than nCPAP, may be
13 recommended over other treatment modalities.

14 15 16 **Compliance with ethical standards**

17
18 **Conflict of interest** All authors declare that they have no conflict of interest.

19
20 **Funding** The current study received no funding.

21
22 **Ethical approval** This study was performed in accordance with the 1964 Declaration
23 of Helsinki. Ethical approval was obtained from the Institutional Review Boards (IRB)
24 of Nagasaki University Hospital (No. 19081916). As this was a retrospective study, the

1 research plan was published on the homepage of the participating hospitals according to
2 the instructions of the IRB in accordance with the guaranteed opt-out opportunity.

3

4 **Informed consent** For this type of study, formal consent is not required.

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Figure Legend

Figure. Changes in the apnea hypopnea index (AHI) from baseline to after oral appliance (OA) therapy. Box plots are displayed for baseline and OA therapy. The 25th and 75th percentiles are represented by the upper and lower margins, the median values by the horizontal black lines. Whiskers represent the maximum value (top) and the minimum value (bottom) of the dataset. Outliers are represented by a dot. (a) The median (interquartile range) of total AHI decreased from 16.1 (11.5-20.2) to 6.5 (3.5-8.6) in the positional obstructive sleep apnea (P-OSA) group ($P<0.001$) and from 17.2 (13.2-24.9) to 8.8 (4.7-13.0) in the non-positional obstructive sleep apnea (NP-OSA) group ($P<0.001$). (b) The median of supine AHI decreased from 23.6 (17.0-34.7) to 7.8 (5.2-12.9) in the P-OSA ($P<0.001$) group and from 19.9 (15.3-24.4) to 12.0 (7.9-18.1) in the NP-OSA group ($P<0.001$). (c) The median of lateral AHI decreased from 3.7 (0.6-9.0) to 1.0 (0-3.6) in the P-OSA group ($P=0.015$) and from 33.7 (18.6-56.6) to 5.9 (3.7-14.4) in the NP-OSA group ($P<0.001$). (d) The median of REM AHI decreased from 23.1 (11.2-37.1) to 11.1 (6.3-18.9) in the P-OSA group ($P<0.001$) and from 33.4 (22.7-49.5) to 16.8 (9.1-26.9) in the NP-OSA group ($P<0.001$). (e) The median of non-REM AHI decreased from 12.6 (8.9-17.7) to 3.6 (2.5-7.7) in the P-OSA group ($P<0.001$) and from 14.8 (7.7-24.3) to 6.3 (1.5-10.5) in the NP-OSA group ($P<0.001$).

Table 1. Characteristics of patients

Characteristics	All patients	P-OSA (n=47)	NP-OSA (n=26)	<i>P</i> value
Age (years), mean $\pm$ SD	57.4 $\pm$ 13.0	59.9 $\pm$ 13.6	53.0 $\pm$ 10.9	0.021
Median (range)	58 (24-82)	61 (24-82)	54 (30-72)	
Sex (Male/Female)	51/22	34/13	17/9	0.599
BMI (kg/m ²), mean $\pm$ SD	24.3 $\pm$ 4.0	23.4 $\pm$ 3.3	25.9 $\pm$ 4.6	0.043
AHI (events/h), mean $\pm$ SD				
Total AHI	19.0 $\pm$ 11.4	17.6 $\pm$ 9.3	21.5 $\pm$ 14.3	0.311
Supine AHI	29.8 $\pm$ 20.3	28.9 $\pm$ 18.7	31.5 $\pm$ 23.1	0.773
Lateral AHI	18.2 $\pm$ 24.4	5.6 $\pm$ 6.2	41.0 $\pm$ 28.4	<0.001
REM AHI	29.7 $\pm$ 18.0	25.7 $\pm$ 16.6	36.9 $\pm$ 18.3	0.011
non-REM AHI	16.3 $\pm$ 12.5	15.6 $\pm$ 10.8	17.7 $\pm$ 15.3	0.890
REM predominant OSA (Yes/No)	51/22	28/19	23/3	0.015

P-OSA: positional obstructive sleep apnea; NP-OSA: non-positional obstructive sleep apnea; SD: standard deviation; BMI: body mass index; AHI: apnea-hypopnea index; REM: rapid eye movement.

Table 2. Multivariate logistic regression analysis of predictors of OA therapy response

Variables	<i>N</i>	Response OR (95% CI)	<i>P</i> value
Age (years)			
<58	36	Reference	
≥58	37	0.213 (0.050-0.902)	0.036
Sex			
Male	51	Reference	
Female	22	1.202 (0.330-4.381)	0.780
BMI (kg/m ²)			
<25	46	Reference	
≥25	27	0.309 (0.089-1.072)	0.064
Positional OSA			
No	26	Reference	
Yes	47	6.544 (1.479-28.950)	0.013
REM predominant OSA			
No	22	Reference	
Yes	51	2.777 (0.689-11.198)	0.151

OA: oral appliance; OR: odds ratio; CI: confidence interval; BMI: body mass index; OSA: obstructive sleep apnea; REM: rapid eye movement.

(a)

(b)

(c)

(d)

(e)