

Risk Factors for Severe Obstructive Sleep Apnea Including Sleeping Position and its Gender Difference : A Retrospective Single-institute Study in Japan

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Purpose : Obstructive sleep apnea (OSA) is a disease characterized by sleep-disordered breathing (SDB) due to upper airway obstruction. Age, body mass index (BMI) and abnormal facial morphology which is evaluated by cephalometry have been reported as risk factors for severe OSA. In addition, the supine sleeping position worsens SDB because it narrows the upper airway. We thought that the percentage of supine position during sleep might be a risk factor for worsening apnea-hypopnea index (AHI) levels but it has not been verified. Therefore, we analyzed that and its gender difference.

Methods : Between May 2008 and May 2020, 228 patients with OSA who underwent full-night polysomnography (PSG) and cephalometry at our hospital were registered retrospectively. We conducted logistic regression analysis using their clinical background, findings on cephalometry and the percentage of supine position during sleep recorded on full-night PSG to identify risk factors for severe AHI levels (≥ 30 events/h). Subsequently, sub-analyses which classified them by gender were performed.

Results : The logistic regression analysis indicated that the percentage of supine position during sleep was a significant risk factor in addition to BMI and the distance from the mandibular plane to the hyoid (MP-H) on cephalometry. A sub-analysis for male patients produced the same results. However, in a sub-analysis for female patients, the risk factors were age and BMI, but not the percentage of supine position during sleep.

Conclusions : The percentage of supine position during sleep is one of the risk factors for severe OSA, but only applies to male patients. *Shinshu Med J 69 : 363–371, 2021*

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Key words : obstructive sleep apnea, sleeping position, gender difference, cephalometry, risk factor

I Introduction

Obstructive sleep apnea (OSA) is a disease caused by the collapse of the upper airway during sleep and is diagnosed through full-night polysomnography (PSG). OSA causes sleep-disordered breathing (SDB), such as apnea and hypopnea, which can lead to intermittent hypoxemia and an increase in sympathetic nerve activity, resulting in daytime sleepiness and

an increased risk of cardiovascular and metabolic disorders¹⁾²⁾. OSA was prevalent in 14 % of men and 5 % of women in a review of the epidemiology³⁾. It is diagnosed by the total number of SDB per hour displayed as the apnea-hypopnea index (AHI). A patient with an AHI level ≥ 5 events/h is diagnosed with OSA and OSA with an AHI level ≥ 30 events/h is considered as severe OSA.

High body mass index (BMI) is an independent risk factor for worsening AHI levels because fat deposition around the upper airway causes airway stenosis⁴⁾.

Old age is also considered a risk factor for OSA because muscle function, related to upper airway

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patency, declines in elderly people, leading to worsening of OSA^{5,6)}. Moreover, sex hormones also contribute to the development of OSA. The ratio of men to women is 2-3:1, and this ratio is maintained regardless of race^{7,8)}. The prevalence of OSA is lower in women than in men before menopause; however, it is similar between sexes after menopause, suggesting that female hormones such as estrogen and progesterone can prevent the collapse of the upper airway^{9,10)}. This is consistent with the report of Bixler et al. that postmenopausal women receiving hormone replacement therapy had a similar prevalence of OSA as premenopausal women¹¹⁾. Therefore, age can be a significant independent factor in women especially.

Abnormal facial morphology is considered as a risk factor. Patients with OSA have a distinctive long face, mandible retraction, lower hyoid bone, and longer soft palate, tending to induce SDB¹²⁾⁻¹⁶⁾. Sakakibara et al. analyzed the characteristics of the upper airway using cephalometry in Japanese OSA patients and showed that they tended to have a longer distance from the mandibular plane to the hyoid (MP-H) on cephalometry¹⁷⁾, which can be a risk factor.

In addition to these factors reported so far, we presume that the supine sleeping position can be related to AHI severity because it strongly affects AHI levels. In general, AHI levels worsen in the supine sleeping position and improves in the lateral sleeping position¹⁸⁾. This is because the supine position can easily narrow the upper airway as it is strongly affected by gravity acting on the soft tissue in the anterior cervical area and tongue; however, the lateral position can suppress the influence of gravity. So, it is possible that the percentage of supine position during sleep contributes to AHI levels although the fact has not been verified so far. Moreover, it may depend on sex because there are some differences in the upper airway structure between the sexes. In a study by Whittle et al., the total neck soft tissue volume was greater and there was greater overall soft tissue loading on the airway in men than in women¹⁹⁾. Nashi et al. reported that males had heavier tongues than females²⁰⁾.

We examined the percentage of supine position during sleep as a risk factor for severe OSA together with the factors reported so far. In addition, the gender difference was also confirmed.

II Materials and Methods

A Participants

Between May 2008 and May 2020, 336 participants with suspected sleep apnea syndrome underwent full-night PSG at our hospital, and 286 patients with an AHI level ≥ 5 events/h were diagnosed with OSA. Among them, 243 patients with OSA who underwent cephalometry were enrolled retrospectively and patients having allergic rhinitis, sinusitis and neuromuscular diseases were excluded. Finally, 228 OSA patients were registered in our study (**Fig. 1**).

The patients' clinical background, results of full-night PSG including the data of sleeping position, and results of cephalometry between non-severe OSA patients (AHI < 30 events/h) and severe OSA patients (AHI ≥ 30 events/h) were analyzed. Statistical analysis was performed to determine the independent risk factors for severe AHI level (≥ 30 events/h). The same analyses were performed as sub-analyses by classifying them into male and female groups.

Our study was approved by the Research Ethics Committee of Shinshu University School of Medicine (approval number: 5083). The study protocols were performed according to the principles outlined in the Declaration of Helsinki of the World Medical Association.

B Cephalometry

The upper airway of the participants was X-rayed from the side area in the standing position (**Fig. 2**)²¹⁾. Skull base length (SN), upper jaw protrusion (\angle SN-A), lower jaw protrusion (\angle SN-B), lower jaw retraction (\angle ANB) and the distance from the mandibular plane to the hyoid (MP-H), which have been shown to be significantly different from those in normal subjects²²⁾⁻²⁴⁾, were measured manually using the electronic medical records system (EV Insite; PSP Inc, Tokyo, Japan).

C Diagnosis of OSA

A PSG device was attached to the participants

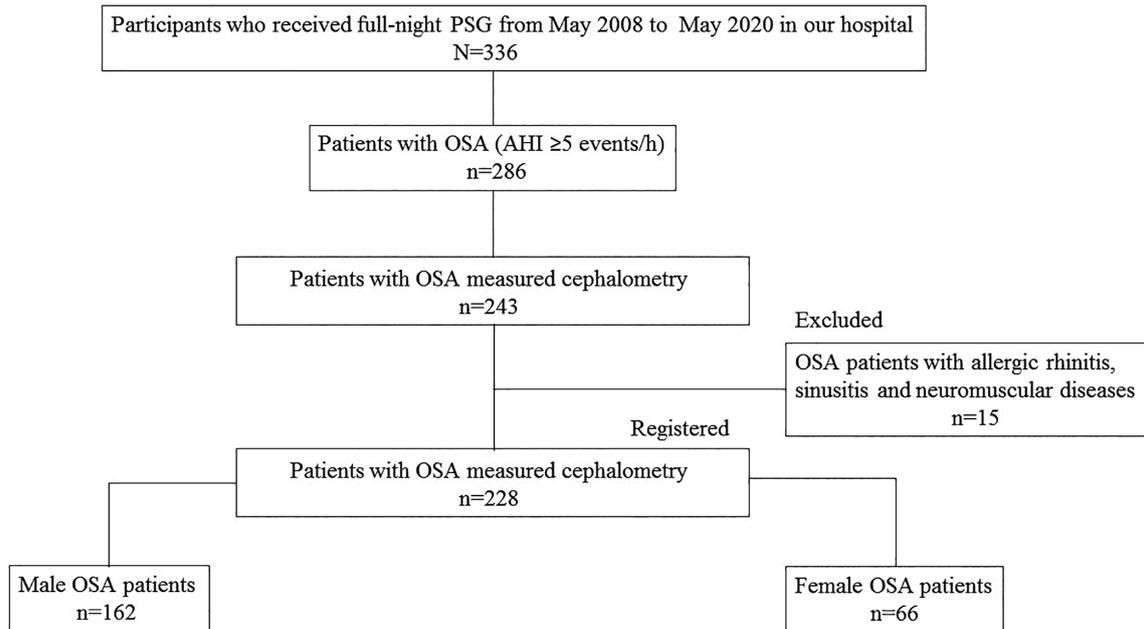


Fig. 1 The process of choosing patients who were registered in our study
Abbreviations : OSA, obstructive sleep apnea ; AHI, apnea-hypopnea index

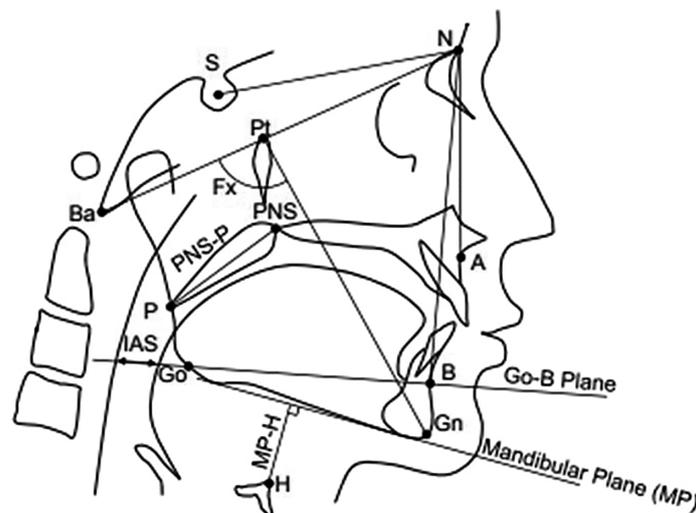


Fig. 2 Cephalometric landmarks with line and area measurements [15]

Abbreviations : S, sella ; N, nasion ; A, A-point, deepest point of maxilla ; B, B-point, deepest point of mandible ; P, palate point ; PNS, posterior nasal spine ; H, superior tip of hyoid bone ; SN, skull base length ; \angle SNA, upper jaw protrusion ; \angle SNB, lower jaw protrusion ; \angle ANB, the length of the soft palate ; MP-H, the distance from the mandibular plane to the hyoid

from 9 : 30 P.M. (lights off) to 6 A.M. (lights on). Full-night PSG examination was performed using Alice 3 (Philips, Amsterdam, Netherlands), which collected data on four-channel electroencephalogram (C4/A1, C3/A2, O2/A1, O1/A2) findings, two-channel electrooculogram findings, submental and leg electromyogram findings, airflow (thermistor and pressure transducer), respiratory effort (chest and abdominal

movement), oxygen saturation, snoring, electrocardiogram findings, and body position. A sleep technician monitored the behavior or sleep position changes of the patients during sleep and manually scored all PSG data, including airflow and respiratory effort, based on the American Academy of Sleep Medicine Manual for the scoring of sleep and associated events²⁵). Respiratory events, including apnea and

hypopnea, were scored according to the “alternative” rule. Apnea was defined as the cessation of respiratory airflow for a minimum of two breaths (10 s). Obstructive apnea was defined as the cessation of airflow with continued respiratory effort (chest and abdominal movement) for the same duration. Hypopnea was defined as a decrease in respiratory airflow of $\geq 50\%$ with $\geq 3\%$ oxygen desaturation or arousal.

D Data analysis

Statistical analysis was performed using SPSS statistics (version 26, IBM, USA). Measurement data were expressed as mean \pm standard deviation values. Comparison of categorical variables was performed using a chi-square test. Comparison of continuous variables was first assessed using a Kolmogorov-Smirnov test to confirm whether they were normally distributed. Subsequently, we confirmed that they had equal or unequal variance using a Levene test. If they were normal and equally distributed, we used a Student's t-test, but if they were normal and had an unequal distribution, we used a Welch's t-test. If they were not normally distributed, we used a Mann-Whitney U test.

We conducted logistic regression analysis selecting “AHI ≥ 30 events/h” as the dependent variable and “age,” “BMI,” and “percentage of supine position during sleep,” and “MP-H” on cephalometry. Statistical significance was set at $p < 0.05$.

III Results

A comparison between the non-severe and severe OSA groups based on the clinical background and the results of full-night PSG including data of sleeping position is shown in **Table 1**. There are significant differences in BMI and some other data of full-night PSG. A comparison of cephalometry results between them is shown in **Table 2**. There is a difference in MP-H. The logistic regression analysis for severe AHI levels indicates that the percentage of supine position during sleep is a significant risk factor for severe OSA, in addition to BMI and MP-H (**Table 3**).

In a sub-analysis about the male group, a comparison between non-severe OSA and severe OSA based on the clinical background and the results of full-

night PSG is shown in **Table 4**. There are differences in BMI, the percentage of supine position during sleep and MP-H. The logistic regression analysis for severe AHI levels indicates that the percentage of supine position during sleep is a significant risk factor for severe OSA, in addition to BMI and MP-H (**Table 5**), which are consistent with the all-gender analysis.

In a sub-analysis about females, a comparison between non-severe and severe OSA based on the clinical background and the results of full-night PSG is shown in **Table 6**. There is a difference in BMI only. The logistic regression analysis for severe AHI levels indicates that age and BMI are risk factors but the percentage of supine position during sleep is not a significant risk factor (**Table 7**).

IV Discussion

Although few papers show the gender difference about risk factors for severe OSA such as clinical background and cephalometry, we are able to do that. The percentage of supine position during sleep was an independent significant risk factor for severe OSA. However, this was not a risk factor for female patients. This indicates that the effect of gravity on upper airway patency differs between the sexes. Marin et al. measured the upper airway dimensions using the acoustic reflection technique in 60 male and 54 female participants in the seated and supine positions and compared the difference between the sexes in the change of the upper airway area by position switch²⁶⁾. They found that male participants had significantly larger decreases in the upper airway area in the supine position than female participants. Their findings were consistent with the gender difference in the genioglossal muscle tone strength reported by Popovic and White²⁷⁾. They reported that females had a greater genioglossal muscle tone than males, suggesting greater defense of their upper airway. The usefulness of positional therapy, which prevents patients from sleeping in the supine position, has been reported²⁸⁾⁻³⁰⁾. Although there is no verification that there is a sex difference in the usefulness of positional therapy, the possibility that it depends on sex could not be excluded. Our study has

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Table 1 Clinical background and results of full-night PSG between non-severe OSA patients (AHI<30 events/h) and severe OSA patients (AHI ≥30 events/h).

Variables	AHI<30 events/h (n = 114)	AHI ≥30 events/h (n = 114)	P-value
Age (years)	59.1 ± 13.1	59.3 ± 13.7	0.90
BMI (kg/m ²)	26.0 ± 4.1	29.0 ± 5.0	<0.001
AHI (events/h)	16.4 ± 7.0	53.7 ± 19.3	<0.001
TST (min)	426.0 ± 83.8	414.7 ± 94.7	0.34
SE (%)	76.3 ± 12.8	75.5 ± 14.5	0.66
REM sleep time (%)	15.0 ± 5.9	11.7 ± 5.9	<0.001
Stage N1 (%)	24.4 ± 13.1	34.2 ± 20.3	<0.001
Stage N2 (%)	54.6 ± 12.2	50.3 ± 18.6	0.044
Stage N3 (%)	6.3 ± 7.4	3.8 ± 5.0	0.030
Percentage of each position during sleep			
Supine position (%)	50.8 ± 23.9	57.3 ± 26.2	0.052
Left lateral position (%)	24.0 ± 20.2	18.7 ± 18.9	0.043
Right lateral position (%)	24.6 ± 21.2	22.3 ± 20.3	0.39
Mean SpO ₂ (%)	94.2 ± 2.0	92.0 ± 2.9	<0.001
Lowest SpO ₂ (%)	80.7 ± 6.8	68.0 ± 13.5	<0.001
3 % ODI (events/h)	14.5 ± 7.1	47.0 ± 21.7	<0.001
CT90 (%)	4.6 ± 11.0	22.7 ± 18.1	<0.001
Arousal index (events/h)	22.7 ± 9.4	47.6 ± 35.3	<0.001
Snoring index (events/h)	59.4 ± 94.0	75.1 ± 60.4	0.33

Data are expressed as mean ± standard deviation (SD)

Abbreviations : PSG, polysomnography ; BMI, body mass index ; AHI, apnea-hypopnea index ; TST, total sleep time ; SE, sleep efficiency calculated by TST/time in bed (%) ; REM sleep time, rapid eye movement sleep time ; SpO₂, oxygen saturation ; 3 % ODI, 3 % oxygen desaturation index ; CT90, total sleep time with SpO₂ under 90 %

Table 2 Findings of cephalometry between non-severe OSA patients (AHI<30 events/h) and severe OSA patients (AHI ≥30 events/h).

Variables	AHI<30 events/h	AHI ≥30 events/h	P-value
SN (mm)	74.4 ± 5.2	74.8 ± 5.7	0.48
∠SNA (°)	58.9 ± 4.6	59.1 ± 3.6	0.37
∠SNB (°)	57.4 ± 4.8	56.1 ± 3.9	0.070
∠ANB (°)	2.5 ± 1.5	3.3 ± 1.6	0.080
MP-H (mm)	15.3 ± 7.7	19.7 ± 6.6	<0.001

Data are expressed as mean ± standard deviation (SD)

Abbreviations : OSA, obstructive sleep apnea ; SN, skull base length ; ∠SNA, upper jaw protrusion ; ∠SNB, lower jaw protrusion ; ∠ANB, lower jaw retraction ; MP-H, the distance from the mandibular plane to the hyoid

Table 3 Results of univariate analysis and logistic regression analysis for severe OSA (AHI \geq 30 events/h)

Variables	Logistic regression analysis	
	P-value	OR (95 % CI)
Age (years)	0.23	1.02 (0.99-1.06)
BMI (kg/m ²)	<0.001	1.22 (1.09-1.37)
Percentage of supine position during sleep (%)	0.017	1.02 (1.01-1.04)
MP-H (mm)	0.0050	1.09 (1.03-1.16)

Abbreviations : OR, odds ratio ; 95 % CI, 95 % confidence interval ; BMI, body mass index ; MP-H, the distance from the mandibular plane to the hyoid

Table 4 Clinical background and results of full-night PSG between non-severe OSA patients (AHI<30 events/h) and severe OSA patients (AHI \geq 30 events/h) in male group

Variables	AHI<30 events/h (n = 79)	AHI \geq 30 events/h (n = 83)	P-value
Age (years)	57.6 \pm 13.5	58.2 \pm 14.9	0.81
BMI (kg/m ²)	26.1 \pm 3.6	28.7 \pm 4.8	<0.001
AHI (events/h)	16.9 \pm 6.8	53.4 \pm 18.2	<0.001
TST (min)	429.1 \pm 81.1	409.7 \pm 96.8	0.17
SE (%)	76.0 \pm 12.6	74.6 \pm 15.4	0.56
REM sleep time (%)	14.9 \pm 5.7	11.5 \pm 7	<0.001
Stage N1 (%)	26.1 \pm 13.6	35.4 \pm 19.6	<0.001
Stage N2 (%)	54.1 \pm 12.7	50.0 \pm 18.5	0.010
Stage N3 (%)	5.1 \pm 5.7	3.1 \pm 4.5	0.015
Percentage of each position during sleep			
Supine position (%)	47.0 \pm 21.1	56.8 \pm 23.9	0.0070
Left lateral position (%)	25.5 \pm 19.7	18.0 \pm 16.8	0.011
Right lateral position (%)	26.5 \pm 21.7	23.6 \pm 20.1	0.37
Mean SpO ₂ (%)	94.3 \pm 1.9	92.1 \pm 2.8	<0.001
Lowest SpO ₂ (%)	80.8 \pm 7.0	67.4 \pm 13.5	<0.001
3 % ODI (events/h)	14.7 \pm 6.8	45.7 \pm 20.1	<0.001
CT90 (%)	4.5 \pm 11.5	22.7 \pm 18.4	<0.001
Arousal index (events/h)	23.4 \pm 9.7	49.0 \pm 39.7	<0.001
Snoring index (events/h)	36.0 \pm 27.8	80.5 \pm 70.0	0.0020
Cephalometry			
MP-H (mm)	15.3 \pm 7.7	19.7 \pm 6.9	0.0082

Data are expressed as mean \pm standard deviation (SD)

Abbreviations : OSA, obstructive sleep apnea ; PSG, polysomnography ; BMI, body mass index ; AHI, apnea-hypopnea index ; TST, total sleep time ; SE, sleep efficiency calculated by TST/time in bed (%) ; REM sleep time, rapid eye movement sleep time ; SpO₂, oxygen saturation ; 3 % ODI, 3 % oxygen desaturation index ; CT90, total sleep time with SpO₂ under 90 % , MP-H, the distance from the mandibular plane to the hyoid

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Table 5 Results of univariate analysis and logistic regression analysis for severe OSA (AHI \geq 30 events/h) in male group

Variables	Logistic regression analysis	
	P-value	OR (95 % CI)
Age (years)	0.66	1.01 (0.97-1.06)
BMI (kg/m ²)	0.018	1.25 (1.04-1.50)
Percentage of supine position during sleep (%)	0.0090	1.03 (1.01-1.06)
MP-H (mm)	0.015	1.11 (1.02-1.20)

Abbreviations : OR, odds ratio ; 95 % CI, 95 % confidence interval ; BMI, body mass index, MP-H, the distance from the mandibular plane to the hyoid

Table 6 Clinical background and results of full-night PSG between non-severe OSA patients (AHI <30 events/h) and severe OSA patients (AHI \geq 30 events/h) in female group

Variables	AHI <30 events/h (n = 35)	AHI \geq 30 events/h (n = 31)	P-value
Age (years)	62.4 \pm 11.6	62.5 \pm 9.3	0.98
BMI (kg/m ²)	25.9 \pm 5.2	29.8 \pm 5.4	0.005
AHI (events/h)	15.3 \pm 7.5	54.6 \pm 21.8	< 0.001
TST (min)	419.0 \pm 89.4	428.1 \pm 87.4	0.68
SE (%)	77.1 \pm 13.2	77.9 \pm 11.4	0.81
REM sleep time (%)	15.2 \pm 6.4	12.5 \pm 6.3	0.12
Stage N1 (%)	20.1 \pm 10.6	30.3 \pm 22.0	0.030
Stage N2 (%)	56.0 \pm 10.5	51.1 \pm 19.1	0.23
Stage N3 (%)	9.5 \pm 9.8	6.1 \pm 5.6	0.11
Percentage of each position during sleep			
Supine position (%)	59.4 \pm 27.4	58.6 \pm 31.4	0.92
Left lateral position (%)	20.6 \pm 20.9	20.5 \pm 23.6	0.98
Right lateral position (%)	20.3 \pm 19.4	18.6 \pm 20.4	0.74
Mean SpO ₂ (%)	94.1 \pm 2.0	92.0 \pm 3.0	< 0.001
Lowest SpO ₂ (%)	80.4 \pm 6.0	70.5 \pm 13.0	< 0.001
3 % ODI (events/h)	14.2 \pm 7.5	50.3 \pm 25.1	< 0.001
CT90 (%)	4.8 \pm 9.6	22.7 \pm 17.3	< 0.001
Arousal index (events/h)	21.2 \pm 8.6	44.4 \pm 21.2	< 0.001
Snoring index (events/h)	97.3 \pm 139.9	63.6 \pm 28.7	0.31
Cephalometry			
MP-H (mm)	11.0 \pm 4.8	15.4 \pm 7.7	0.058

Data are expressed as mean \pm standard deviation (SD)

Abbreviations: OSA, obstructive sleep apnea ; PSG, polysomnography ; BMI, body mass index ; AHI, apnea-hypopnea index ; TST, total sleep time ; SE, sleep efficiency calculated by TST/time in bed (%) ; REM sleep time, rapid eye movement sleep time ; SpO₂, oxygen saturation ; 3 % ODI, 3 % oxygen desaturation index ; CT90, total sleep time with SpO₂ under 90 %, MP-H, the distance from the mandibular plane to the hyoid

Table 7 Results of univariate analysis and logistic regression analysis for severe OSA (AHI \geq 30 events/h) in female group

Variables	Logistic regression analysis	
	P-value	OR (95 % CI)
Age (years)	0.036	1.11 (1.01-1.21)
BMI (kg/m ₂)	0.0080	1.32 (1.08-1.63)
Percentage of supine position during sleep (%)	0.40	1.01 (0.99-1.04)
MP-H (mm)	0.21	1.09 (0.95-1.24)

Abbreviations : OR, odds ratio ; 95 % CI, 95 % confidence interval ; BMI, body mass index ; MP-H, the distance from the mandibular plane to the hyoid

the limitation that the study cohort included a rather small number of female patients (66 females vs. 162 males) as our study was performed at a single institute.

In conclusion, the percentage of supine position during sleep is a risk factor for severe OSA ; however, this is not the case for female patients.

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