We investigated differences in the depth of hypoxia produced by apneic events of the same duration (30 seconds) amongst patients with different degrees of OSAS according to their AIs (apnea indices). The relationship between apnea duration (seconds) and fall in oxygen saturation (%) was evaluated by means of a linear regression analysis. The fall induced by a 30-second apnea event was designated as the "oxygen desaturation value 30" (ODV30). We analyzed the polysomnographic recordings of 122 OSAS patients who showed significant correlations (p<0.01) between apnea duration and subsequent fall in oxygen saturation and calculated their respective ODV30.

We evaluated the influence of AI and BMI on ODV30 by multi-comparison and found out that standardized partial regression coefficients of BMI and AI were 0.578 and 0.148, respectively (multi-regression analysis, SPSS). BMI was proved to be more influential on ODV30 than AI was.

On the other hand, the ODV30 of mild, moderate and severe OSAS patients was $8.84 \pm 2.62\%$ (Mean ± S.D.), $8.25 \pm 2.45\%$ and $10.59 \pm 3.32\%$, respectively.

Our study shows that fall in oxygen saturation is particularly extensive in severe OSAS patients and that fall in oxygen saturation is deepened as obesity increases.

We think ODV30 is a useful variable for evaluating OSAS.

**Key words:** Apnea duration, hypoxia, cardiovascular complication, sleep apnea syndrome, overweight, body mass index

**Introduction**

The hallmark of obstructive sleep apnea syndrome (OSAS) is intermittent apnea during sleep. When apnea continues for some period of time, hypoxia occurs subsequently. The longer the apnea, the greater the fall in arterial oxygen saturation. Severe hypoxia is known to play a key role in producing serious cardiovascular organ damage.

Marin et al.\(^1\) demonstrated that severe OSAS places patients at increased risk for fatal and non-fatal cardiovascular events. A high rate of cardiovascular complications might well be expected because hypoxia can inflict irreversible damage on cardiac muscle.
The purpose of this study is to investigate the severity of oxygen desaturation in OSAS patients and compare it amongst the patients with mild, moderate and severe OSAS.

In addition, other possible factors affecting a fall in arterial oxygen saturation are assessed.

**Materials and Methods**

Changes in airflow through the nose or the mouth were detected by thermistor and changes in transcutaneous oxygen saturation (SpO₂) were determined by pulse oximetry during polysomnographic examinations. Apnea was defined as more than 90% reduction of airflow amplitudes which continued for more than 10 seconds. In general, severity of OSAS is classified based on the number of apnea and hypopnea per one hour (apnea-hypopnea index: AHI). However, the definition of hypopnea is not distinct. Thus, hypopnea was not adopted as a variable for detection of a fall in oxygen saturation in this study. Our classification of severity of OSAS is different from the ordinary classification that is based on AHI. We used apnea index (AI: number/hour) as a variable instead of AHI, because AI was regarded as a more useful variable to evaluate oxygen desaturation induced by interruption of breathing. In our study, the ranges of AI classifying the severity into three groups simulated the range of the ordinary classification: 5 ≤ mild OSAS < 15, 15 ≤ moderate OSAS < 30, and severe OSAS ≥ 30.

Polysomnographic examinations were carried out at Ikebukuro Sleep Center in collaboration with Tokyo Medical and Dental University Graduate School. An Alice 4 Sleep Diagnostic System (Respironics, U.S.A.) was used as an apparatus for polysomnography (PSG). We evaluated the relationship between apnea duration (in seconds) and the fall in oxygen saturation (%) at apneic events. Apneic event was followed by oxygen desaturation with a time lag which was inconsistently across patients. The fall in oxygen saturation (desaturation %) was reported as the difference between the initial oxygen saturation level at the onset of an apneic event and the deepest point of the following desaturation curve.

We reviewed polysomnographic recordings of consecutive one hundred and forty patients at Ikebukuro Sleep Center and analyzed the correlations between apnea duration and subsequent falls in oxygen saturation (Excel, MicroSoft). We excluded eighteen patients who showed p>0.01 from the study. Most of these patients showed high incidence of central apnea events, mixed apnea events and unstable recordings of PSG. We designated the oxygen desaturation per 30 seconds of apnea as “oxygen desaturation value 30” (ODV30) and used it for this study. It was calculated according to the formula “y=ax+b”, which was determined by a linear regression analysis (Excel, MicroSoft) (Figure 1).

We analyzed the polysomnographic recordings of one hundred and twenty-two OSAS patients and calculated their respective ODV30. They included one hundred and eleven men and eleven women, aged 23 - 80 years. We classified our study patients into three groups by the severity of their OSAS—mild (38 cases, aged 23 – 80 years, 49.9 ± 15.3 years, 5 ≤ AI < 15), moderate (33 cases, aged 23 – 71 years, 45.9 ± 12.4 years, 15 ≤ AI < 30) and severe (51 cases, aged 23 – 79 years, 45.1 ± 12.8 years, AI ≥ 30) groups. We compared ODV30 among those three groups (Bonferroni’s multiple comparison: SPSS for Windows: version 15.0, SPSS Inc, Chicago IL, USA).

We additionally evaluated the correlation between ODV30 and body mass index (BMI: kg/m²) and between ODV30 and age by means of scatterplot (Excel, MicroSoft).

The relationship between BMI and AI was also statistically analyzed (Excel, MicroSoft). We used multiregression analysis (SPSS) for the statistical evaluation in order to compare the influence of BMI and AI on ODV30.

Finally, we matched 11 male and 11 female patients for BMI and age, and then we compared the ODV30 between male and female (Student’s t-test for independent samples). In this study, the number of female patients is much smaller than that of male patients. This is attributed to the fact that the number of female OSAS patients is generally about 1/10 of the number of male OSAS patients. The data which were used in this study were obtained by regular PSG recordings for the diagnosis of SAS in clinical setting at Ikebukuro Sleep Center and analyzed from another viewpoint of hypoxia. Therefore, the study was conducted in accordance with the Declaration of Helsinki.

**Results**

The ODV30 of mild, moderate, and severe OSAS groups was 8.84 ± 2.62% (Mean±S.D.), 8.25 ± 2.45% and 10.59 ± 3.32%, respectively (Figure 2). The slight difference between the ODV30 of patients in the
mild or the moderate OSAS groups was not statistically significant. The larger differences in ODV30 between the mild and the severe groups, and between the moderate and severe groups were statistically significant (p<0.01). The association between ODV30 and BMI was analyzed and shown in Figure 3. ODV30 was significantly correlated with BMI (p<0.01).

As far as influence of BMI and AI on ODV30 is concerned, the standardized partial regression coefficients of BMI and AI were 0.578 and 0.148, respectively and multiple correlation coefficient (R) and coefficient determination (R²) were 0.657 and 0.432, respectively (multi-regression analysis, SPSS).

On the other hand, there was no correlation between age and ODV30 (r = -0.17, p> 0.05). A significant correlation was shown between BMI and AI (r = 0.441, p< 0.01) (Figure 4).

No significant difference appeared between the ODV30, 8.28±1.91% (Mean±S.D.), in male and
ODV30, 9.52±2.52%, in female (Figure 5).

Discussion

OSAS is elicited by intermittent obstruction of the upper airways during sleep. It is pointed out that the nose, nasopharynx, soft palate and tongue play important roles in narrowing the upper airways during sleep. Thus, OSAS is induced by adenoid hypertrophy, palatal tonsil hypertrophy, mandible hypoplasia or some abnormal facial skeletons. Obesity deposits fat in the tissue lining the upper airways and reduces the size of the airways. Obesity plays an important role in causing OSAS.

In this study, we used “apnea” instead of “apnea-hypopnea” in order to evaluate the change of oxygen saturation. The reason why we used “apnea” is that hypopnea induces various levels of decline in oxygen saturation, even if the hypopneic events continue for the same period of time. Hypopnea is defined as more than 50% reduction of airflow with more than 3% fall of oxygen saturation or with arousal. Hypopnea means 60% reduction of airflow, 70% reduction of airflow, or 80% reduction of airflow as well during sleep. In addition, AHI also includes the number of hypopnea which is not followed by definite oxygen desaturation, but only followed by arousal. Therefore, changes of oxygen saturation are not proportional to the changes of hypopneic duration.

The concept, “hypoxia tolerance time”, has been already studied in the field of anesthesiology. Jense et al. preoxygenated patients for 5 minutes after inducing anesthesia with muscle relaxation and allowed them to remain apneic until arterial saturation as measured by pulse oxymetry reached 90%. The authors found out that the time taken for oxygen saturation to decrease to 90% was significantly reduced in obese patients than in normal subjects. They proved that obesity is the important factor affecting oxygen desaturation.

As far as we ranged over an extensive literature, there has not been any report evaluating the oxygen tolerance of SAS patients under no general anesthesia by means of a single variable such as ODV30. ODV30 is of clinical importance, because this variable can be calculated on the basis of ordinary PSG recordings alone.

As hypoxia deepens, subjects are more susceptible to the cardiac muscle damage. If subjects have same AHI, the subject with greater BMI is more susceptible to cardiac muscle damage than the subject with less BMI. In addition to obesity, severity of OSAS is considered to affect the susceptibility to the cardiac muscles damage, because ODV30 is increased in severe OSAS patients (Figure 2).

We evaluated the patients classified by AI according to ordinary AHI classification. The mild, moderate and severe groups expressed 32.89±16.02 (Mean±S.D.), 42.60±12.70, and 74.56±12.70 of AHI, respectively. Thus, our classification by AI underestimates the severity of OSAS comparing with the ordinary AHI classification. However, it is shown that AHI increases as OSAS progresses from mild to moderate, and from moderate to severe. In addition, statistical differences are found amongst those three groups. We consider that AI deserves attention as a variable for evaluating oxygen desaturation.

Our study clarified, by multi-regression analysis, that the standardized partial regression coefficient of BMI is larger than that of AI (BMI:0.578, AI:0.148). As shown in Figure 3, The spots of mild, moderate and severe OSAS patients show similar ranges of distribution. However, most of the patients with ODV30>15% are occupied by severe OSAS patients, shown as green spots. BMI is proved to be more influential on ODV30 than AI.

As far as the factors affecting ODV30 are concerned, there may be other unknown factors rather than obesity and severity of OSAS, because there are some subjects that show rather small BMI or less severity, but show large ODV30.

OSAS has been implicated as a risk factor in hypertension, stroke, and myocardial infarction. According to Baquet et al., the severity of oxygen desaturation appears to be one of the best predictors for carotid wall thickening and plaque occurrence in OSAS patients without known cardiovascular disease. Intermittent hypoxia is said to alter chemoreflexive control of muscle - sympathetic nerve activity (MSNA), and sustain the elevation of blood pressure. Intermittent hypoxia seems to be an important cause of cardiovascular and neurovascular complications in OSAS patients.

Marin et al. observed that the risk of fatal and non-fatal cardiovascular events is increased in severe OSAS patients. As shown in Figure 4, AI is correlated with BMI (r=0.441, p<0.01). This finding suggests that OSAS becomes severe, as BMI increases.

Apnea during sleep can induce hypoxia, as can breath holding during wakefulness. Both conditions look similar from the standpoint of interrupted breathing. Strohl and Altose determined the rate of fall in arterial oxygen saturation (SaO2) in six healthy subjects during
breath-holding and concluded that the fall in oxygen saturation in OSAS patients was greater during obstructive sleep apneas than during breath-holding in wakefulness. They argued that repeated apneas lower the oxygen saturation baseline in OSAS. This may explain partially the apparent greater fall in oxygen saturation in asleep versus wakeful subjects. If, as our study suggests, excess weight predicts decreased oxygen saturation in patients with severe OSAS, baseline oxygen lowering may play an interactive role.

Nakano et al. suggested that the degree of desaturation at an apneic event was significantly affected by the degree of obesity. This is an important observation on the relationship between obesity and oxygen desaturation. But they did not show how to evaluate the oxygen desaturation of each OSAS patient.

Our determinations clearly show that weight should always be taken into consideration when we discuss the pathophysiology of severe OSAS. Wolks et al. suggested that the coexistence of OSAS and obesity has widespread implications for cardiovascular dysfunction in obese individuals and that it contributes to the clustering of abnormalities broadly defined as the metabolic syndrome. We have found that in severe OSAS, an accelerated ODV30 is significantly correlated with BMI in our study.

This is probably attributed to the fact that obese subjects have elevated work of breathing, respiratory muscle insufficiency and reductions in respiratory ventilations affecting arterial oxygen saturation. Oxygen saturation is affected by functional residual capacity (FRC) and total lung capacity (TLC). Watson and Pride demonstrated that reduced FRC and TLC are consistently found in obese patients. Obesity probably restricts the movement of the thoracic cage and diaphragm and reduces FRC and TLC. We have shown ODV30 is an objective measure of susceptibility to hypoxia in severe OSAS and independent of age and gender differences. When patients with severe OSAS are overweight, the oxygen desaturation they experience per apneic episode is proportionately greater. It exceeds that suffered by normal weight patients with similar apneic indices, again independent of age and gender.

ODV30, the fall in oxygen saturation per 30-seconds of apnea, appears to be a useful and informative parameter to evaluate severity of OSAS and particularly important in the study of cardiovascular risk in severe OSAS patients.

References