Effect of Sleep Position and Sleep Stage on the Collapsibility of the Upper Airways in Patients with Sleep Apnea

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Abstract: Collapsibility of the upper airways has been identified as an important pathogenic factor in obstructive sleep apnea (OSA). Objective measures of collapsibility are pharyngeal critical pressure (Pcrit) and resistance of the upstream segment (Rus). To systematically determine the effects of sleep stage and body position we investigated 16 male subjects suffering from OSA. We compared the measures in light sleep, slow-wave sleep, REM sleep and supine vs. lateral positions. The pressure-flow relationship of the upper airways has been evaluated by simultaneous readings of maximal inspiratory airflow (Vimax) and nasal pressure (p-nCPAP). With two-factor repeated measures ANOVA on those 7 patients which had all 6 situations we found a significant influence of body position on Pcrit ($p<0.05$) whereas there was no significant influence of sleep stage and no significant interaction between body position and sleep stage. When comparing the body positions Pcrit was higher in the supine than in the lateral positions. During light sleep Pcrit decreased from 0.6 ± 0.8 cm H_2O (supine) to –2.2±3.6 cm H_2O (lateral) ($p<0.01$), during slow-wave sleep Pcrit decreased from 0.3±1.4 cm H_2O (supine) to –1.7±2.6 (lateral) ($p<0.05$) and during REM sleep it decreased from 1.2±1.5 cm H_2O to –2.0±2.2 cm H_2O ($p<0.05$). Changes in Rus revealed no body position nor sleep-stage dependence. Comparing the different body positions Rus was only significantly higher in the lateral position during REM sleep ($p<0.05$). The results indicate that collapsibility of the upper airways is not mediated by sleep stages but is strongly influenced by body position. As a consequence lower nCPAP pressure is needed during lateral positions compared to supine positions.

Key words: Critical closing pressure; upper airway resistance; collapsibility; sleep stages; body position

INTRODUCTION

THE PROMINENT PATHOMECHANISM OF OBSTRUCTIVE SLEEP APNEA (OSA) IS PARTIAL OR COMPLETE OBSTRUCTION OF THE UPPER AIRWAYS DURING SLEEP WITH CONCOMITANT OXYGEN DESATURATION.[1] The collapse of the upper airways is modified by a number of factors. Anatomical abnormalities of the upper airways can decrease airway space and reduce airflow.[2,3,4] Other factors are altered neuromuscular control of pharyngeal muscles which are responsible for keeping the pharynx open and a general reduction of skeletal muscle tone during sleep.[4,5]

Experiments have shown that it is possible to induce upper airway collapse by applying an external negative pressure to mouth and nose.[6] This can be regarded as an implication of the Starling resistor, a model for collapsible tubes which has been applied to the upper airways.[7] The Starling resistor consists of a thin-walled elastic tube enclosed in a chamber in which the pressure can be greater than the pressure inside the tube.[8] In patients with obstructive sleep apnea less negative pressure is needed to create a collapse of the upper airways compared to normal individuals.[6,9] This increased collapsibility in OSA patients can be caused by an anatomical narrow pharynx, by an altered reflex response or a changed neuromuscular control. With a change of body position during sleep these factors may also change.

The importance of body position in the pathogenesis of sleep apnea has been pointed out in several studies. In many patients the number of apneas observed was lower in the lateral position compared to the supine position.[10,11]

As sleep depth modifies skeletal muscle tone an influence on upper airway muscles could be expected. Previous studies suggest that the collapsibility of the upper airways during light sleep and REM sleep is higher than during slow-wave sleep even if skeletal muscle tone is lower during slow-wave sleep.[12,13,14] This can be the result of an extension of the site of obstruction towards lower levels of the oropharynx.[15]

In our study we investigated the influence of sleep stage (light sleep, slow-wave sleep, and REM sleep) and body position (lateral and supine position) and their interaction on Pcrit and Rus by evaluating the pressure-flow relationship in 16 male patients with OSA.

METHODS

Patients

Sixteen male patients who consulted the sleep laboratory due to excessive daytime sleepiness and a positive screening test for sleep apnea were recruited. Only patients with an indication for nCPAP therapy according to a diagnostic polysomnographic night study and after a completed nCPAP titration night in the sleep laboratory were asked to enter this study. Patients with abnormal upper airways, obstructive or restrictive lung diseases

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Table 1—Patient data and results of diagnostic apnea/hypopnea index and nCPAP pressure as obtained during the first titration night

Patient	Age [years]	Height [cm]	Weight [kg]	BMI [kg/m2]	AHI [n/h]	nCPAP [cm H2O]
1	60	171	100	34.2	54.4	9
2	44	180	100	30.9	26.3	10
3	56	174	120	39.6	65.2	8
4	61	181	103	31.4	35.0	8
5	32	181	130	39.7	44.0	9
6	52	172	80	27.0	32.0	9
7	59	173	75	25.1	48.0	10
8	61	172	85	28.7	36.0	10
9	49	179	97	30.3	48.0	11
10	58	184	114	33.7	72.0	11
11	37	168	145	51.4	98.3	13
12	61	172	117	39.5	63.0	9
13	34	190	133	36.8	67.9	13
14	43	180	82	25.3	47.2	10
15	46	168	88	31.1	59.0	7
16	55	169	78	27.3	76.3	10
$\overline{X}$	50.5	175.9	102.9	33.3	48.9	9.8
s.d.	10.1	6.4	21.6	6.9	19.2	1.6

$\overline{X}$ = mean value, s.d. standard deviation

were excluded. Age ranged from 32 to 61 years (mean: 50.5±10.0 years) and BMI ranged from 25 to 51 kg/m2 (mean: 33.3±6.9 kg/m2). The diagnostic study revealed an apnea/hypopnea index of 48.9±19.2 events/hour. During the treatment study on the following night nCPAP titration was performed in order to eliminate all apneas and hypopneas. The resulting nCPAP pressures ranged from 7 to 13 cm H2O (mean: 9.8±1.6 cm H2O). For this study patients underwent an additional night in the sleep laboratory. Anthropometric and diagnostic data are listed in Table 1.

Measurements

Polysomnography was performed according to standard criteria.[16] Respiratory effort was recorded by esophageal pressure (Gaeltec, Dunvegan, England). Respiratory movements were recorded by respiratory inductive plethysmography (Studley data systems, Oxford, England) and airflow was recorded with a lightweight pneumotachograph (CP100, Bicore, Irvine, Calif. USA) installed between the nasal mask and the nCPAP tube. As this type of pneumotachograph has a non-linear pressure-flow relationship, of which the characteristics are encoded in the plug of the sensor, a dedicated amplifier (Biscope, Singh Medical, Stäfa, Switzerland) was used to obtain a calibrated linear flow signal. During the study a nBiPAP system (BIPAP STD-30, Respironics, Murrysville, USA) was used to apply positive pressure and a modified nCPAP ventilator (Somnotron, Weinmann, Hamburg, Germany) was used to apply negative pressure. An electronic switch allowed a quick change of applied pressure between either one of the two ventilators or room pressure. All polygraphic and respiratory signals were calibrated at the start of the test and were recorded by a paper polygraph and a computer for later processing. Body position was monitored by an infra-red video camera. A lateral position was scored if the head of the patient did lie on the side and if not more than one shoulder kept contact with the mattress. Flexing the head was not enough to score lateral position. Left and right were pooled to one lateral position.

Assessment of Pcrit and Rus

The analysis of the pressure-flow relationship of the upper airways allows to determine collapsibility of the upper airways and their resistance upstream to the site of collapse. This can be done because it is assumed that any pharyngeal obstruction is caused by an imbalance between the pressure inside the pharyngeal segment of the airways and the pressure in the environment which is composed of tissue pressure and tone of the pharyngeal wall muscle. When the pressure in the airways downstream to the pharyngeal segment is lower than the environmental pressure and lower than the nasal pressure, the pharyngeal walls flutter and limit maximal inspiratory airflow as formulated by the starling resistor which is a model for a collapsible tube.[16,17] If the intraluminal pressure drops below a critical pressure (Pcrit), the upper airways collapse and airflow ceases.

As long as the upper airways allow airflow to pass they can be characterized by their resistance, which is mainly determined by the upstream resistance Rus. The maximal inspiratory airflow Vimax is given by the pressure-flow relationship:

$$Vimax = (Pn - Pcrit) / Rus$$

where Pn is the nasal pressure, measured upstream of the collapsible segment. Assuming that Pcrit and Rus are in a steady state, a drop of Pn will cause a drop of Vimax.

The pressure-flow relationship was produced on a computer using the digital recordings of calibrated airflow and nasal pressure. Pcrit and Rus were determined for light sleep (sleep stage 2), slow-wave sleep (sleep stage 3 and 4) and REM sleep in different body positions. Maximum inspiratory airflow Vimax was evaluated at different nasal pressure levels. To do this, Pn was lowered progressively in runs for three to four breaths (fig. 1). The runs with lowered pressure were separated by at least one minute of undisturbed sleep. Flow limitation was observed as a flattening of inspiratory airflow as soon as nasal pressure dropped below the environmental pressure of the collapsible segment. At the same time an increase in respiratory effort was

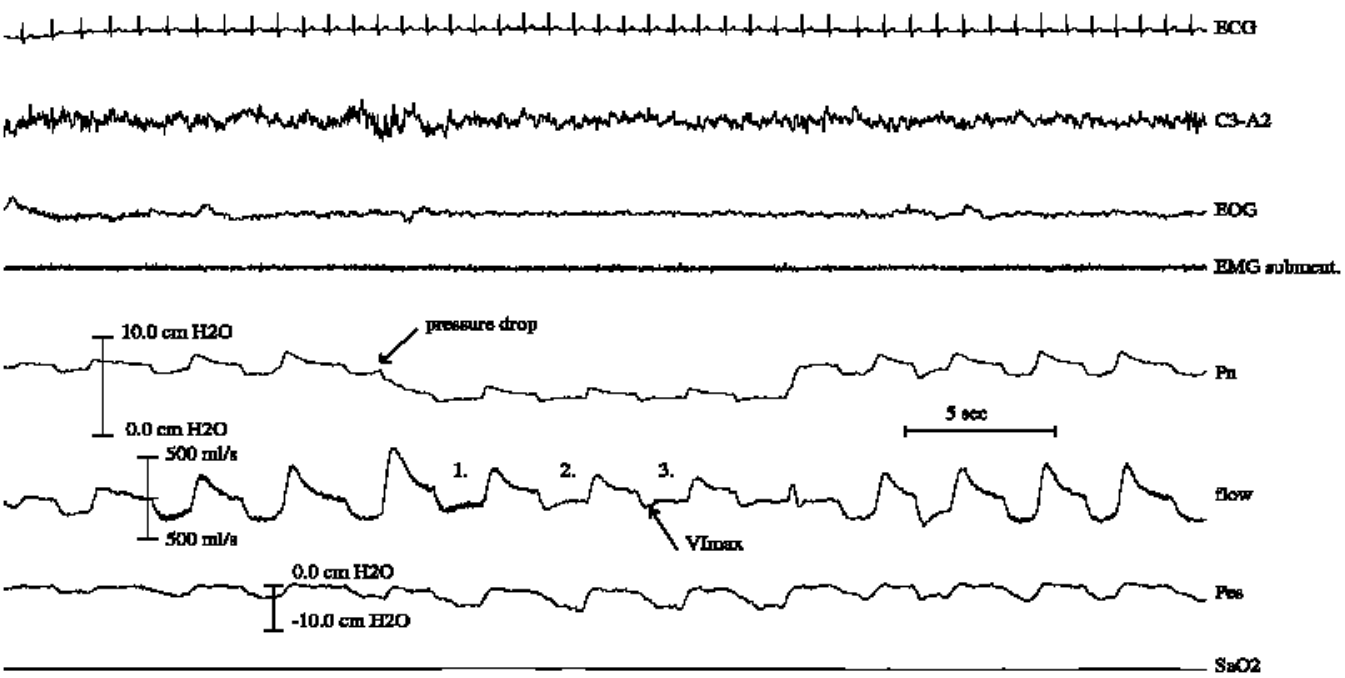

Figure 1—The recording illustrates the assessment of Pcrit and Rus by dropping the effective nCPAP pressure for four breaths. The first three breaths are numbered. Negative deflections of flow indicate inspiration. Inspiratory flow limitation can be recognized by the flattening of the curve. The pressure drop and the value used for the determination of VImax are indicated.

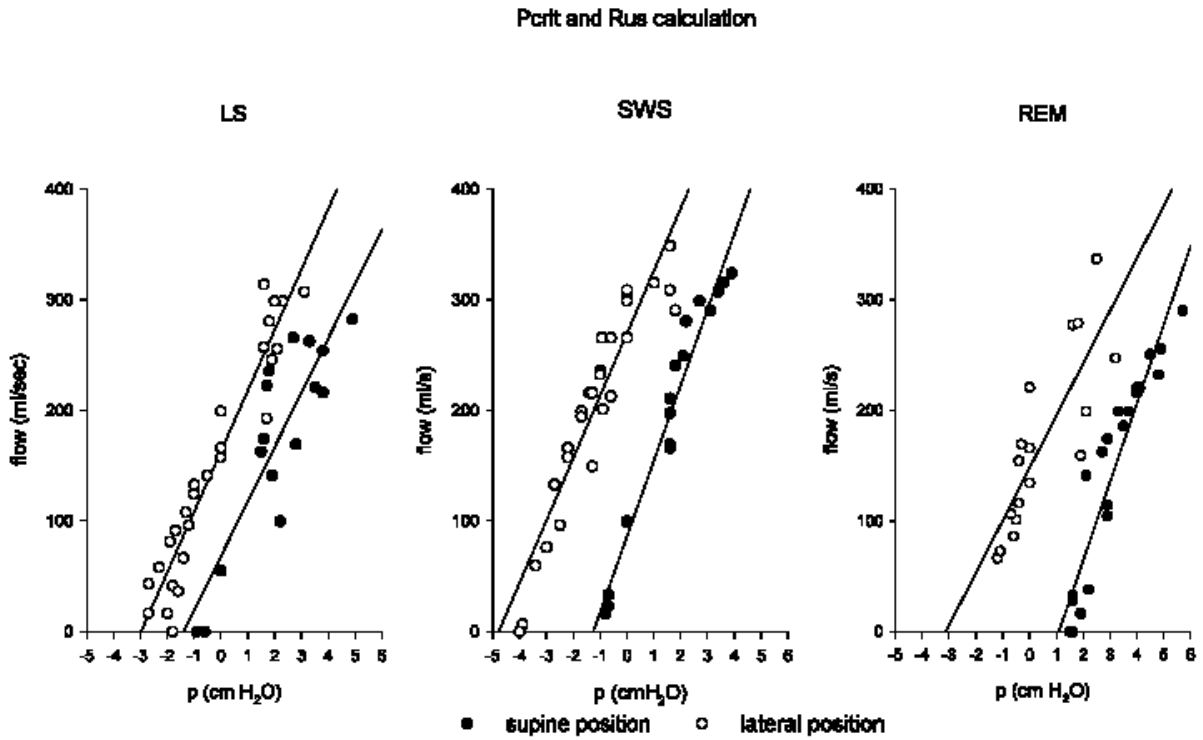

Figure 2—Pcrit and Rus values were determined using the Vimax vs. Pn graph. Linear regression was calculated for each condition. All six conditions (LS=light sleep, SWS=slow-wave sleep, REM sleep; lateral and supine position) were shown in this figure.

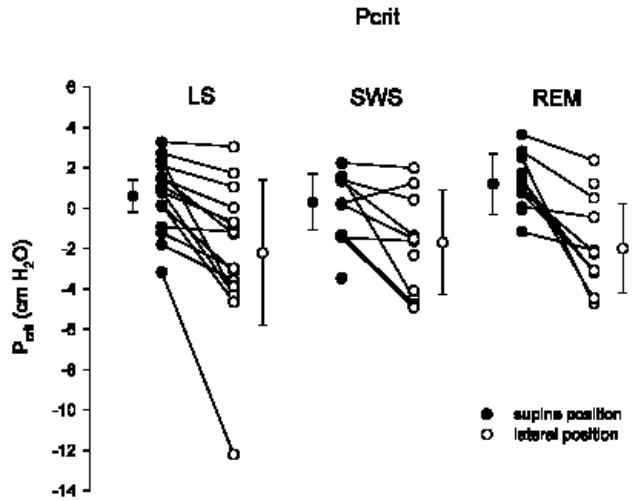

Figure 3—A significant decrease of Pcrit on changes of body position can be observed for all sleep stages. On the left side is the supine position and on the right side is the lateral position. The individual and mean values with standard deviation are plotted.

observed by increased negative pressure swings of esophageal pressure. The more the nasal pressure was lowered the less maximal inspiratory flow remained. Nasal pressure was lowered until no flow was recorded for three to four subsequent respiratory cycles. If the lowering of nCPAP pressure did not suffice to obtain a zero-flow, negative pressure was applied for the three to four breaths. If the patient woke up, we waited until regular breathing re-established under full nCPAP pressure.

We required a minimum of ten runs to determine Pcrit. Flow limitation was determined for the third breath after the decrease of Pn.[4] Pcrit was defined as the intercept of the pressure-flow regression line and the pressure-axis at Vimax=0 of the measurements taken (Figure 2). The regression analysis was performed using Sigmaplot 5.0 for Windows® (SPSS Inc., Chicago). The Pcrit value was accepted only if the linear regression turned out to be significant ($p<0.01$), which corresponds to a minimal regression coefficient of $r=0.71$. Rus is given by the inverse of the slope of the regression line. Measurements were separated according to sleep stage and body position. Group values are given as means±standard deviation. To investigate the interaction between sleep stages and body position a two-factor repeated measures ANOVA was carried out using SPSS 9.0 for Windows. Statistical tests for differences between body positions were performed using the Wilcoxon ranked sign test for non-normally distributed data. A statistical significance level of $p<0.05$ was regarded as significant for all tests.

RESULTS

In all 16 patients we tried to determine Pcrit in all body positions. All except one patient slept on their back. Not all sleep stages were found in all body positions. For a total of 78 combinations of sleep stage and body position we were able to determine valid Pcrit values. As two-factor repeated measures ANOVA requires the presence of all conditions with respect to body position and sleep stage, only seven subjects fulfilled this requirement. ANOVA showed no significant interaction between sleep stages and body position. ANOVA revealed a significant effect of body position on Pcrit whereas the effect of sleep stage on Pcrit remained to be non significant. In order to investigate this effect further, we tested the differences between body positions for sleep stages separately. During light sleep Pcrit was determined in 15 patients and was reduced from 0.6±0.8 cm H_2O to –2.2±3.6 cm H_2O significantly ($p<0.01$) with a change from supine to lateral position. During slow-wave sleep Pcrit was determined in 9 patients and was reduced from 0.3±1.4 cm H_2O to –1.7±2.6 cm H_2O significantly ($p<0.05$). During REM sleep Pcrit was determined in 10 patients and was reduced from 1.2 ± 1.5 cm H_2O to –2.0±2.2 cm H2O significantly ($p<0.05$). Individual and mean values are presented in Figure 3.

Rus was evaluated whenever it was possible to determine Pcrit. Thus, the same groups of patients were used. The two-factor repeated measure ANOVA did not reveal any significant influence of body position nor sleep stage. During light sleep Rus changed from 18.3±6.4 cm H_2O / l*s to 19.9±9.9 cm H_2O / l*s from supine to lateral position. During slow-wave sleep Rus changed from 16.8±8.1 cm H_2O / l*s to 16.3±6.3 cm H_2O / l*s. During REM sleep Rus increased from 14.8±3.7 to 22.1±9.1 cm H_2O / l*s from supine to lateral position significantly ($p<0.05$). Individual and mean values are presented in Figure 4.

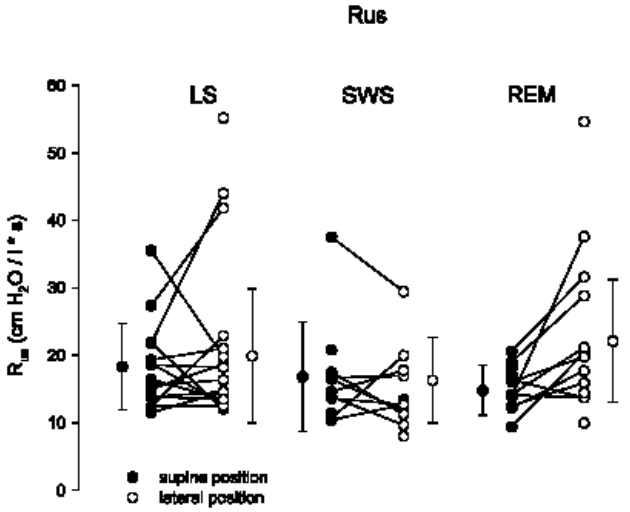

Figure 4—Individual Rus values and their changes for body positions are plotted for all sleep stages. Only during REM sleep a significant change ($p<0.05$) was noted. Mean values are presented together with standard deviation.

DISCUSSION

In this study we investigated the influence of sleep stage and body position on upper airway collapsibility (Pcrit) and resistance upstream to the site of pharyngeal collapse (Rus) in 16 male patients with obstructive sleep apnea.

The most important result of this study is the significant effect of body position on Pcrit whereas the effect of sleep stage remained to be non-significant. In addition there was no significant interaction between body position and sleep stage. Comparing the effect of body position on collapsibility of the upper airways during all sleep stages a significant reduction from

supine to lateral position was found. No significant effects were found for upper airway resistance values.

To determine Pcrit values in the lateral position we had to apply negative pressure in most cases. Therefore, it has to be considered that the negative pressure applied to the upper airways might cause a reflex activation of pharyngeal dilator muscles[18] which in turn reduces Pcrit values. Therefore, the influence of sleep stages on the negative Pcrit values obtained for lateral positions has to be interpreted with caution.

Pcrit was evaluated using the third breath after the decrease in Pn according to Schwartz.[4] In some patients there is a progressive collapse beyond the third breath (compare figure 1). Then a third breath may not adequately define the ultimate tendency of the airway to collapse.

Our results give some evidence that upper airway collapsibility in either lateral or supine position is not effected by sleep stage. We could show a significant reduction of Pcrit comparing the supine with the lateral position. Whereas the overall mean of Pcrit in the supine position was positive the overall mean of Pcrit in the lateral position was negative and confirms the results of Issa[17] and Neill.[19] Our results show that this finding remains true for all sleep stages investigated. In terms of absolute values Issa showed larger changes of upper airway collapsibility as a result of a change in body position compared to changes in sleep stages. As the change in body position was evaluated in three patients only, the effects of sleep stage and body position were not compared in his study. Neill found relatively little change of upper airway collapsibility when comparing supine with lateral position in six patients. Significant changes were found with upper body elevation during sleep. In the study of Neill again too few patients were left in order to compare upper airway collapsibility with sleep stage and body position.

Our results confirmed the results of Schwartz[4] who also found no significant differences in Pcrit between sleep stages. Thus our results are in contrast to Issa[17] who found higher collapsibility during light sleep and REM sleep than during slow-wave sleep. In view of the clinical observation, that there are more apneas during REM sleep than during slow-wave sleep, this result may be surprising. We consider Pcrit being more a measure of mechanical properties of the upper airways, which change with body position but not with sleep state. The observation of having more apnea during REM sleep and during light sleep may be related more to an instability in the control of breathing. This interpretation can not be final since REM sleep is a variable sleep stage during which upper airway collapsibility may vary from breath to breath. If this is the case then the technique used to determine Pcrit for the third breath would not be adequate.

The reduction of pharyngeal collapsibility in the lateral position can be due to several mechanisms. As the tongue may play a role in upper airway obstruction[1,20] the lateral position can have a protective function by preventing the tongue from occluding the airway when the genioglossus muscle is hypotonic. According to investigations in cats the tongue has only a small influence on Pcrit.[21]

A reduction of Pcrit can be also caused by a reduction of the environmental pressure in the tissue. This may be due to a change in shape and length of the trachea when lying on the side[22] and thus cause an increase in the tension of the mucosa of the pharyngeal segment.[23] We hypothesize that the main contribution of the change of Pcrit with body position from back to lateral is caused by a change of the shape of the collapsible segment of the upper airways during sleep. This follows the thoughts of Leiter who emphased the importance of upper airway shape.[24] Unfortunately neither Leiter nor our data can give full evidence of this specific hypothesis. Our results strongly support the hypothesis that Pcrit is more determined by mechanical factors influencing the upper airways than neuromuscular factors.[4]

We also investigated the resistance upstream of the site of collapse Rus by the inverse of the pressure-flow relationship during all sleep stages and body positions. This is a numerically calculated value which is used in several studies, although it is not well validated and results have to be interpreted with care. Observed values are similar to the results of Schwartz[4] but relatively high compared to Sforza[25] which may be due to patient selection. Surprisingly Rus was higher in the lateral position during REM sleep. This may indicate that Rus is controlled by additional factors which have not been investigated well enough until now. We interpret this result very cautious because the concept of resistance in a system with a collapsible tube modeled by a Starling resistor is very problematic, because the pressure-flow relationship cannot be characterized by a single value. We choose the Rus value because it is the only conventional measure to describe the pressure-flow relationship of the upper airways.

The evaluation of Pcrit of the upper airways on the basis of the pressure-flow relationship allows us to objectify the collapsibility of the upper airways. Sleep stage effects on collapsibility seem to play a minor role compared to body position. We could show that a change from the supine to the lateral body position increased the stability of the upper airways considerably. This can explain the reported body position dependent apnea. This also implies that effective CPAP pressure in the lateral position can be remarkably lower than in the supine position. This has to be considered in titration studies and CPAP control studies.

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REFERENCES

1. Remmers JE, Groot WJ, Sauerland EK, Anch AM. Pathogenesis of upper airway occlusion during sleep. J Appl Physiol 1978;44:931-938.
2. Horner RL, Mohiaddin DG, Lowell S, Shea ED, Burmann ED, Longmore DB, Guz A. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnea and weight matched controls. Eur Respir J 1989;2:613-622.
3. Mortimore IL, Marshall I, Wraith PK, Sellar RJ, Douglas NJ. Neck and total body fat deposition in nonobese and obese patients with sleep apnea compared with that in control subjects. Am J Respir Crit Care Med 1998;157:280-283.
4. Schwartz AR, O'Donnell CP, Baron J, Schubert N, Alam D, Samadi SD, Smith PL. The Hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular acitivity. Am J Respir Crit Care Med 1998;157:1051-1057.
5. Hudgel DW, Suratt PM. The human airway during sleep. In: Saunders NA, Sullivan CE. Sleep and breathing. New York: Dekker, 1994:191-208.
6. Schwartz AR, Smith PL, Wise RA. Induction of upper airway occlusion in sleeping individuals with subathmospheric nasal pressure. J Appl Physiol 1988;64:535-442.

7. Smith PL, Wise RA, Gold AR, Schwartz AR, Permutt S. Upper airway pressure-flow relationships in obstructive sleep apnea. J Appl Physiol 1988;64:789-795.
8. Lambert RK, Wilson TA. Flow limitation in a collapsible tube. J Appl Physiol 1972;33:150-153.
9. Issa F, Sullivan CE. Arousal and breathing responses to airway occlusion in healthy sleeping adults. J Appl Physiol 1983;55:1113-1119.
10. Cartwright RD. Effect of sleep position on sleep apnea severity. Sleep 1984;7:110-114.
11. Pevernagie DA, Shepard JW. Relations between sleep stage, posture and effective nasal CPAP levels in OSA. Sleep 1992;15:162-167.
12. Schäfer T, Schläfke ME. Zusammenspiel von Schlaf und Atmung: Untersuchungen zur Atmungsregulation im Schlaf. Somnologie 1997;1:21-26.
13. Boudewyns AN, Van de Heyning PH, Backer WA. Site of upper airway obstruction in obstructive apnea and influence of sleep stage. Eur Respir J 1997;10:2566-2572
14. Horner RL. Motor control of the pharyngeal musculature and implications for the pathogenesis of obstructive sleep apnea. Sleep 1996;19:827-853.
15. Gold AR, Schwartz AR. The pharyngeal critical pressure: The whys and hows of using nasal continous positive airway pressure diagnostically. Chest 1996;110:1077-1088.
16. Phillipson EA, Remmers JE. American Thoracic Society consensus conference on indications and standards for cardiopulmonary sleep studies. Am Rev Respir Dis 1989;139:559-568.
17. Issa F, Sullivan CE. Upper airway closing pressure in obstructive sleep apnea. J Appl Physiol: Respirat Environ Exercise Physiol 1984;57:520-527.
18. Mathew OP. Upper airway negative-pressure effects on respiratory activity of upper airway muscles. J Appl Physiol 1984;56:500-504.
19. McKenzie Neill A, Angus SM, Sajkow D, McEvoy RD. Effects of sleep posture on upper airway stability in patients with obstructive sleep apnea. Am J Respir Crit Care Med 1997;155:199-204.
20. McEvoy RD, Sharp DJ, Thornton AT. The effects of posture on obstructive sleep apnea. Am Rev Respir Dis 1986;133:662-666.
21. Rowley JA, Permutt S, Willey SJ, Smith PL, Schwartz AR. Effect of tracheal and tongue displacement on upper airway airflow dynamics. J Appl Physiol 1996;80:2171-2178.
22. Thut DC, Schwartz AR, Roach D, Wise RA, Permutt S, Smith PL. Tracheal and neck position influence upper airway dynamics by altering airway length. J Appl Physiol 1993;75:2084-2090.
23. Van de Graaf WB. Thoracic influence on upper airway patency. J Appl Physiol 1988;65:2124-2131.
24. Leiter JC. Upper Airway Shape. Is it important in the pathogenesis of obstructive sleep apnea? Am J Respir Crit Care Med 1996;153:894-898.
25. Sforza E, Petiau C, Weiss T, Thibault A, Krieger J. Pharyngeal critical pressure in patients with obstructive sleep apnea syndrome. Am J Crit Care Med 1999;159:149-157.