Obstructive sleep apnea (OSA) is caused by intermittent closure of the upper airway during sleep. Although the pathogenesis of OSA remains unclear, it is now known that apnea is related to increases in upper airway collapsibility during sleep. With increasing levels of upper airway collapsibility, greater degrees of airflow obstruction have been observed in patients with asymptomatic snoring and in those with recurrent hypopneas and apneas. These early observations led us to conclude that upper airway collapsibility varies widely over the spectrum from health to disease, and that increases in upper airway collapsibility play a central role in the pathogenesis of OSA.

In our previous studies, a pressure-flow relationship was constructed during sleep from which upper airway collapsibility and resistance upstream to the site of collapse could be inferred. This pressure-flow relation-
ship was used to define upper airway collapsibility as the level of nasal mask pressure ($P_m$) below which the upper airway closed (critical closing pressure [$P_{crit}$]) and the upstream resistance ($R_n$) as the inverse of the slope of the pressure-flow relationship. Using these methods, we subsequently demonstrated that patients experienced an improvement in their apnea whenever $P_{crit}$ declined sufficiently after weight loss or uvulopalatopharyngoplasty. These observations led us to suggest that quantitative measurements of $P_{crit}$ and its response to specific therapeutic maneuvers could help predict the treatment response in polysomnographic indexes of apnea severity.

Nevertheless, assessing the upper airway response to therapeutic maneuvers remained difficult because $P_{crit}$ and $R_n$ had to be inferred from pressure-flow relationships generated during periods of stable sleep. Our previous studies used a lengthy protocol to establish a pressure-flow relationship from multiple measurements of tidal airflow taken over a wide range of $P_m$ during prolonged periods of stable sleep. Clearly, without methods for rapidly constructing such a pressure-flow relationship, it is not possible to determine $P_{crit}$ and $R_n$ repeatedly under various test conditions within a single night. Before this approach could be put into clinical practice, therefore, it became necessary to streamline the methods for acquiring pressure-flow data and for assessing $P_{crit}$ and $R_n$ with precision.

We developed an abbreviated method for generating upper airway pressure-flow relationships from multiple breaths during sleep. This method involved assessing responses in tidal airflow to brief rather than prolonged perturbations in $P_m$. In our initial study, however, we found that airflow did not reach a steady-state level within the first three breaths after an abrupt reduction in $P_m$. In the present study, therefore, we allowed more time to establish steady-state levels of airflow by lowering $P_m$ for up to six breaths. With this protocol, we hypothesized that (1) airflow would reach a steady-state level within a specific number of breaths; (2) steady-state airflow levels could be used to construct a pressure-flow relationship from which $P_{crit}$ and $R_n$ could be determined; and (3) these variables could be estimated with sufficiently narrow confidence intervals (CIs) to discern differences in upper airway function between different body positions and sleep stages.

**Materials and Methods**

**Patient Selection**

Ten patients with OSA were recruited for this study from the Sleep Disorders Unit at the University Hospital Antwerp, Belgium. They were considered eligible if the respiratory disturbance index (RDI) during nonrapid eye movement (NREM) sleep was > 10 episodes/h. Patients with any concurrent medical illnesses except hypertension were excluded. The Local Review Board of the Antwerp University Hospital approved the protocol for which all patients gave informed consent.

**Study Design**

Each patient underwent baseline full-night polysomnography (PSG) to characterize the severity of sleep-disordered breathing during NREM and rapid eye movement (REM) sleep (see “Baseline PSG” below). Thereafter, patients underwent an additional night of PSG to assess upper airway function during sleep (see “Experimental Protocol” below).

**Baseline PSG**

**Recording Methods:** Standard PSG techniques were used to characterize patients at baseline and during the experimental protocol. In brief, physiologic variables were continuously recorded including EEG ($C_1/A_1, C_2/A_2$), electro-oculogram, chin muscle electromyogram and electromyogram of anterior tibialis muscle, and ECG. Snoring was measured with a microphone placed at the suprasternal notch. A body position sensor attached to a thoracic belt was used to monitor body position. Oxygen saturation was measured by pulse oximetry (Palco Laboratories; Santa Cruz, CA). Tidal airflow was monitored with a thermocouple or full face mask connected to a pneumotachometer (279331; Hamilton Medical; Reno, NV). A balloon probe (Medtronic Upper Airway; Maastricht, The Netherlands) connected to a pressure transducer (Response III; Medtronic Upper Airway; Minneapolis, MN) measured esophageal pressure as previously described. The signals from the esophageal balloon were used to measure respiratory effort. All physioologic signals were digitized at a frequency of 100 Hz, and stored for further analysis (Windaq200; Dataq Instruments; Akron, OH).

**Analysis:** Sleep stage analysis of nocturnal PSGs was performed visually according to the criteria outlined by Rechtschaffen and Kales. A 3-s definition for arousal was used, as per the American Academy of Sleep Medicine. Apnea was defined by the complete absence of oronasal airflow for at least 10 s. Apneas were classified as obstructive, mixed, or central according to standard criteria. Hypopnea was defined as a > 50% decrease in oronasal airflow accompanied by a ≥ 4% drop in oxygen saturation from baseline or an arousal from sleep. The RDI was calculated as the total number of apneas and hypopneas per hour of sleep for both NREM and REM sleep, and separately for the time that the patient slept supine and in the lateral recumbent position.

**Upper Airway Assessment**

An additional full-night PSG was performed for the purpose of assessing upper airway function during sleep as described in the experimental protocol below. For this protocol, patients were fitted with a nasal mask (nasal continuous positive airway pressure [CPAP] mask; Respironics Inc; Murraysville, PA) as above. A chin strap was used to minimize leakage of air through the mouth when necessary. Airflow was measured with a pneumotachometer that was connected to the nasal mask and a pressure transducer (Sefam; Vandoorn-le-Nancy, France). $P_m$ was measured with a similar pressure transducer connected to a port in the nasal mask. The nasal mask was connected via a breathing circuit and a bidirectional valve to a positive pressure source (Tranquility Plus; Healthdyne Technologies; Marietta, GA) and a negative pressure source (modified Rem-Star unit; Respironics).
Pn was set within the positive range by altering the flow delivered by the CPAP device through the breathing circuit. When Pn was lowered into the negative pressure range, the level of subatmospheric pressure was preset in the negative pressure source. The bidirectional valve was then switched, thereby connecting the negative pressure source to the breathing circuit. Thereafter, the valve was switched back to restore a positive Pn.

**Experimental Protocol**

During the experimental protocol, each patient was allowed to initiate sleep while lying either supine or in the lateral recumbent position with a single pillow placed under the head. During sleep, Pn was increased stepwise every 5 min as previously described until inspiratory airflow limitation (see definition below) was abolished. The holding pressure was then defined as the lowest level of Pn required to eliminate inspiratory airflow limitation. This pressure corresponded to the minimally "effective CPAP pressure" and to the "upper airway opening pressure," as previously described by other investigators. This level of holding Pn was then maintained throughout the protocol.

During periods of stable NREM (stage II to IV) or REM sleep, Pn was lowered abruptly during an inspiration, as illustrated in Figure 1. Pn was then raised to holding pressure, and lowered repeatedly every 1 to 2 min to discrete levels encompassing the level at which airflow became zero. If arousal occurred, the patient was allowed to reestablish stable sleep before continuing the experimental protocol. Runs spanned a range of approximately 6 cm H2O range in Pn and a range of zero to approximately 400 mL/s in maximal inspiratory airflow (V\text{\text{max}}).

After patients initiated sleep, pressure-flow data were acquired initially for either the supine or lateral recumbent position during NREM sleep. Thereafter, the patient was repositioned from the supine to lateral recumbent position (or vice versa), and another NREM data set was collected in this body position. In those patients who maintained sleep, a final data set was acquired during REM sleep in the supine position. Throughout this protocol, special care was taken to assure that patients lay either completely supine or in the lateral recumbent position.

**Data Analysis**

With each step decrease in Pn, up to six consecutive breaths were analyzed (Fig 1). Initially, PSG signals were examined to detect any arousal from sleep during each run. Runs were excluded from analysis when they precipitated an arousal or sleep stage transition within the first 20 s of lowering the Pn or occurred during stage I NREM sleep. Otherwise, all breaths after reductions in Pn were analyzed until either six breaths or an arousal had occurred. Each of these breaths was then assessed for the presence or absence of inspiratory airflow limitation. For each flow-limited breath, V\text{\text{max}} and Pn were measured. The level of V\text{\text{max}} was computed as the difference in airflow between the onset of the inspiratory effort (see negative deflections in esophageal pressure in Fig 1) and the inspiratory flow maximum.

Pressure and flow values were tabulated and used for all subsequent analysis. Data were also categorized based on body position and sleep stage (NREM and REM).

**Definition of Flow Limitation:** Initially, the inspiratory airflow and esophageal pressure signals were examined to determine whether inspiratory airflow limitation had occurred. Inspiratory airflow limitation was defined by the development of a V\text{\text{max}} as the pressure gradient across the airway continued to increase. In practice, we determined this gradient to be increasing whenever the esophageal pressure continued to fall progressively beyond the

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**Figure 1.** Representative pressure and flow recordings during a step decrease in Pn in NREM sleep. Six breaths are shown when Pn is lowered from 12 cm H2O holding pressure to 4 cm H2O. Note that the airflow signals shifted abruptly downward during the step decrease in Pn, reflecting a decrease in the level of bias flow through the breathing circuit. Pes = esophageal pressure.
point of V\textsubscript{\textit{max}}. We recognized, however, that the esophageal pressure swing may have overestimated the driving pressure across the upper airway by an amount equal to the change in lung elastic recoil pressure during lung inflation. A change in recoil pressure of approximately 2.5 cm H\textsubscript{2}O was estimated from end-expiration to end-inspiration if a tidal volume of approximately 0.5 L and lung compliance of approximately 0.2 L/cm H\textsubscript{2}O was assumed. Allowing for variations in tidal volume and lung compliance between breaths and patients, respectively, airflow limitation were considered to be present for a given inspiration whenever the esophageal pressure fell beyond the point of V\textsubscript{\textit{max}}. This definition of inspiratory airflow limitation was then taken to be the criterion for establishing the presence of airflow limitation in all flow-limited inspirations that were analyzed during periods of reduced P\textsubscript{n}.

\textbf{Breath-to-Breath Analysis:} The breath-to-breath response in V\textsubscript{\textit{max}} to step decreases in P\textsubscript{n} was analyzed with a two-factor analysis of variance (ANOVA; repeated measures design for responses to breath number and P\textsubscript{n} level). Separate ANOVAs were performed for data obtained in the supine and lateral recumbent positions within NREM sleep. For these ANOVAs, breath number and P\textsubscript{n} level were considered as within subject (repeated measures) factors for six breath numbers and five P\textsubscript{n} levels, respectively. Post hoc analysis (Scheffé test) was then used to establish statistical significance between levels within factors. Additional post hoc comparisons were made to investigate the interaction between breath number and P\textsubscript{n}.

\textbf{Pressure-Flow Relationships (Perit and R\textsubscript{N}):} In each patient, the relationship between V\textsubscript{\textit{max}} and P\textsubscript{n} was examined for specific breaths after step reductions in P\textsubscript{n}. Least squares linear regression was computed to examine the response in V\textsubscript{\textit{max}} to changes in P\textsubscript{n} for each experimental condition (ie, body position and sleep stage). The regression equation was then solved for Perit, which was defined as the P\textsubscript{n} below which V\textsubscript{\textit{max}} became zero. R\textsubscript{N} was also calculated as the reciprocal of the slope of this regression equation, as previously described.

The CIs for Perit and R\textsubscript{N} were calculated as follows. The inverse regression method\textsuperscript{4} was used for generating 95\% confidence bands around the V\textsubscript{\textit{max}} vs P\textsubscript{n} regression line. The intersections of the upper and lower confidence bands with the P\textsubscript{n} axis (where V\textsubscript{\textit{max}} becomes zero) provide the lower and upper 95\% fiducial limits for Perit, respectively. The 95\% CIs for R\textsubscript{N} were computed as the reciprocal of the upper and lower limits of the 95\% CI for the slope of the regression equation, V\textsubscript{\textit{max}} vs P\textsubscript{n}. To investigate the effect of body position and sleep stage on Perit and R\textsubscript{N}, Wilcoxon matched pairs tests were performed. Pearson’s correlation coefficient was calculated to examine the relationship among Perit, R\textsubscript{N}, RDI, and body mass index (BMI). Statistical analysis was performed using Statistica (version 5; Stat Soft; Tulsa, OK). Data are presented as mean (± SD). Statistical significance is accepted at p < 0.05.

\section*{Results}

\textbf{Patient Characteristics}

Anthropometric, pulmonary function, and PSG data at baseline are presented in Table 1. Patients included in this study were middle-aged obese men.
who had PSG evidence of severe OSA (NREM RDI, 61.7 ± 7.0 episodes/h). No patient was hypoxemic (PaO₂ < 65 mm Hg) or hypercapnic (PaCO₂ > 45 mm Hg) during wakefulness. Moreover, no significant change in BMI or neck circumference occurred between baseline and experimental PSG. BMI was 32.0 ± 5.6 kg/m² and 32.0 ± 5.8 kg/m², respectively.

**Variables of Upper Airway Function**

**Table 1—Baseline Anthropometric, Spirometric, and PSG Data***

<table>
<thead>
<tr>
<th>Variables</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>53.3 ± 8.2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>32.0 ± 5.6</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>42.8 ± 2.2</td>
</tr>
<tr>
<td>PaO₂ wakefulness, mm Hg</td>
<td>53.1 ± 8.6</td>
</tr>
<tr>
<td>PaCO₂ wakefulness, mm Hg</td>
<td>30.1 ± 2.3</td>
</tr>
<tr>
<td>TLC, % predicted</td>
<td>101.8 ± 5.7</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>95.8 ± 11.7</td>
</tr>
<tr>
<td>Total sleep time, min</td>
<td>382.1 ± 60.0</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>76.7 ± 13.4</td>
</tr>
<tr>
<td>NREM time, min</td>
<td>338.6 ± 70.7</td>
</tr>
<tr>
<td>REM time, min</td>
<td>46.7 ± 65.8</td>
</tr>
<tr>
<td>RDI episodes/h</td>
<td>63.0 ± 14.6</td>
</tr>
<tr>
<td>RDI NREM, episodes/h</td>
<td>61.7 ± 7.0</td>
</tr>
<tr>
<td>RDI REM, episodes/h</td>
<td>55.2 ± 15.6</td>
</tr>
</tbody>
</table>
| Mean SaO₂, %                            | 92.0 ± 2.8

*Data are presented as mean ± SD. TLC = total lung capacity.

Effect of Body Position: Having demonstrated stable levels of Vmax for the third through fifth breaths, we then constructed Vmax vs Pn relationships from data obtained in the supine and lateral recumbent positions, as illustrated in Figure 2 for a representative patient. From these relationships, the Pcrit and Rn, and the CIs around these variables, were calculated, as represented in Table 3.

When comparing Pcrit in the supine to lateral recumbent position, we found that Pcrit fell from 1.8 ± 1.5 cm H₂O (mean CI, 0.1 to 2.7 cm H₂O) to −1.1 ± 2.6 cm H₂O (mean CI, −1.8 to 0.4 cm H₂O) (p = 0.009) in NREM sleep, respectively. This resulted in a mean fall in Pcrit of 2.9 ± 2.0 cm H₂O in the lateral recumbent position (Fig 3). In Figure 4, the Pcrit CIs are displayed for both body positions and show no overlap in four patients (patients 2, 3, 4, 5).

**Analysis of Vmax Responses to Step Decreases in Pn**

Step decreases in Pn yielded pressure-flow data for the supine and lateral recumbent positions in NREM sleep for 18.5 ± 5.2 runs and 15.6 ± 3.2 runs, respectively. For this total number of 34.1 ± 6.5 runs, flow-limited breaths were encountered in 68.7 ± 17.3%, and arousal was induced in 12.3 ± 10.7% of runs. The total elapsed time during which data were acquired for supine and lateral recumbent positions was 3.6 ± 1.2 h (range, 1.5 to 5.2 h). In REM sleep, pressure-flow relationships for the supine position were constructed from data accumulated over 7.8 ± 2.2 runs, of which 84.3 ± 13.2% contained flow-limited breaths and 13.9 ± 9.8% induced arousal. The total elapsed time for REM data acquisition was 0.8 ± 0.6 h.

After step decreases in Pn during NREM sleep, we observed significant alterations in Vmax within the six ensuing breaths for supine (F = 11.5; degrees of freedom [df]ₕ = 5; p < 0.001) and lateral recumbent (F = 9.9; df = 5; p < 0.001) positions. *Post hoc* analysis revealed no significant differences in Vmax for the third through fifth breaths in either the supine or lateral recumbent position. Rather, we found that Vmax for these breaths was significantly lower than that for the first and second breaths in the supine position, and lower than the first and sixth breaths in the lateral recumbent position. Stated otherwise, our findings indicate that Vmax fell to a quasisteady-state level for the third through fifth breaths after step decreases in Pn in both body positions (Table 2).

In addition to the main effect of breath number, ANOVA confirmed that Pn had a statistically significant influence on Vmax (F = 7.3; df = 4; p < 0.001; and F = 8.2; df = 4; p < 0.001) for supine and lateral recumbent positions, respectively. Finally, a significant interaction between Pn and breath number for both the NREM supine and lateral recumbent conditions (F = 5.2; df = 20; p < 0.001; and F = 3.0; df = 20; p < 0.001) was demonstrated. Specifically, we found that the breath-to-breath differences in Vmax were most pronounced at lower Pn levels. We conclude from the analysis that breath-to-breath changes in Vmax occurred in response to step reductions in Pn, particularly at the lowest pressure levels, but that Vmax in the third through fifth breaths reached a quasisteady state.

**Table 2—Vmax (± SD) for NREM Breath 1 Through 6 in the Supine and Lateral Recumbent Positions**

<table>
<thead>
<tr>
<th>Breaths</th>
<th>Supine</th>
<th>Lateral Recumbent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>262.2 ± 50.1*</td>
<td>267 ± 41.0†</td>
</tr>
<tr>
<td>2</td>
<td>265.8 ± 61.4*</td>
<td>201.1 ± 32.2†</td>
</tr>
<tr>
<td>3</td>
<td>210.2 ± 61.3</td>
<td>183.8 ± 42.4</td>
</tr>
<tr>
<td>4</td>
<td>210.5 ± 85.2</td>
<td>188.6 ± 53.3</td>
</tr>
<tr>
<td>5</td>
<td>211.2 ± 46.6</td>
<td>213.7 ± 74.7</td>
</tr>
<tr>
<td>6</td>
<td>244.8 ± 57.3</td>
<td>236.8 ± 70.8†</td>
</tr>
</tbody>
</table>

*p < 0.001 vs breaths 3 to 6 in supine position.
†p < 0.001 vs breaths 3 to 5 in lateral recumbent position.
and 6), indicating a significant positional effect on Pcrit in these patients. In the remaining six patients, the lack of a significant positional effect is suggested by overlap of CIs. Such overlap is largely attributed to either minimal differences in the Peri (patients 7, 8, 9, and 10) or to relatively large CIs (patients 1 and 5). In contrast to the positional responses in Peri, no significant difference in Rn was detected with positional maneuvers.

**Effect of Sleep Stage:** In Table 4, Pcrit and Rn and their respective CIs are described for five patients sleeping in the supine position in NREM and REM sleep. In these patients, we found no significant difference in Peri (1.8 ± 1.5 cm H2O; mean CI, 0.1 to 2.7 cm H2O vs 1.6 ± 2.3 cm H2O; mean CI, 1.9 to 2.8 cm H2O) or Rn (16.0 ± 7.5 cm H2O/L/s; mean CI, 11.6 to 27.5 cm H2O/L/s; vs 14.3 ± 8.8 cm H2O/L/s; mean CI, 8.4 to 13.2 cm H2O/L/s) for NREM vs REM sleep, respectively. Whereas an overall effect of sleep stage was not discerned, a significant effect on Peri in patient 3 and on Rn in patients 2 and 3 was detected because the CIs around these variables did not overlap in these patients.

**Relationship Between Pcrit and RDI**

Concerning the relationship between the Pcrit changes and RDI, the NREM RDI did not change significantly between the supine and lateral recumbent positions (70.6 ± 15.6 episodes/h vs 59.3 ± 33.6 episodes/h, respectively; p = 0.07) for the group as a whole. On subgroup analysis, however, we found that the NREM apnea index fell significantly from 52.8 ± 25.7 episodes/h in the supine position to 30.8 ± 24.5 episodes/h (p = 0.03) in the lateral recumbent position for those patients with a subatmospheric Pcrit in the lateral recumbent position (n = 6). In contrast, the NREM hypopnea index did not change significantly between the supine and lateral recumbent positions (16.8 ± 15.2 vs 19.5 ± 10.9 episodes/h, respectively).

In this subgroup, the decrease in apnea index in the lateral recumbent position can be attributed to an increase in Vi max from 0.0 ± 0.0 to 88.2 ± 106.2 mL/s when these patients were breathing at atmospheric Pn in the supine and lateral recumbent positions, respectively. Finally, the RDI, apnea index, and hypopnea index did not change in patients whose Pcrit remained above atmospheric in the lateral recumbent position (n = 4). These findings are consistent with the notion that the response in RDI and its component apnea and hypopnea indexes depend on the level to which Pcrit falls (see “Discussion”).

Regarding sleep stage–related changes in Pcrit, we found no significant change in RDI between NREM and REM sleep (60.8 ± 18.2 vs 54.6 ± 8.6 episodes/h, respectively; n = 5). Moreover, no significant correlation existed between changes in Peri and RDI in response to alterations in either body position or sleep stage. Rather, a significant correlation between the lateral recumbent Peri and RDI (p = 0.04) and between the supine Peri and BMI (p = 0.001) was found.

**DISCUSSION**

In this study, we developed an abbreviated, standardized method for characterizing upper airway function during sleep by examining pressure-flow relationships for the upper airway in patients with OSA. These relationships were constructed from breaths obtained after lowering Pn abruptly from a relatively high holding pressure level. When several breaths were evaluated after step reductions in Pn,
we found that the level of $V_{\text{max}}$ fell to a relatively low level within the first three breaths and remained stable at this level through the fifth breath. Having demonstrated a quasisteady-state response in airflow for breaths three through five, we then used these breaths to construct pressure-flow relationships for NREM (supine and lateral recumbent position) and REM (supine only) sleep. From these relationships, we characterized two variables of upper airway function—$P_{\text{crit}}$ and $R_n$—both of which determine the severity of airflow obstruction during sleep. With repeated measurements of these variables, our methods allowed us to discern small decreases in $P_{\text{crit}}$ as patients moved from supine to lateral recumbent position. When determinations of CI around $P_{\text{crit}}$ were examined, we found that a $R_n, \text{H}_2\text{O}/\text{L/s}$ significant positional difference in $P_{\text{crit}}$ was evident within 4 of 10 of our patients. In contrast, no consistent positional change in $R_n$ was detected, and little significant sleep stage–related change in either

**Figure 3.** $P_{\text{crit}}$ is illustrated for each patient in the supine and lateral recumbent positions in NREM sleep ($n = 10; p = 0.009$).
Pcrit or Rn was discerned in the patients who were able to maintain REM sleep during the protocol. We conclude that our methods for delineating upper airway pressure-flow relationships during sleep allow for multiple precise NREM determinations of Pcrit within a single night under different test conditions.

Our approach to studying upper airway function during sleep builds on previous studies of upper airway pressure-flow relationships. In the previous work, a single pressure-flow relationship was constructed from multiple breaths obtained at several levels of Pn during prolonged periods of stable sleep.15 Although this approach allowed investigators to delineate differences in Pcrit among groups with varying degrees of upper airway obstruction during sleep, it did not afford them the opportunity to make repeated measurements of Pcrit and Rn under several experimental conditions in one patient within a single night. To investigate the variability in upper airway function within a single night, it was necessary to develop precise methods for constructing several pressure-flow relationships during different sleep stages and body positions. Such comparisons required that data acquisition be streamlined; yet the data had to reflect steady-state responses of the upper airway to specific test conditions. Initially, an abbreviated method was piloted in which Pn was lowered repeatedly from a holding pressure for three consecutive breaths.7 In this study, we found that V˙{\text{max}} decreased steadily over these three breaths, leading us to conclude that a steady-state pressure-flow relationship could not be constructed from these breaths. We therefore extended the period during which Pn was lowered, and found that a

Table 4—Pcrit and Rn in NREM and REM Sleep (Supine Position)*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Pcrit, cm H\textsubscript{2}O</th>
<th>RN, L/s</th>
<th>Pcrit, cm H\textsubscript{2}O</th>
<th>RN, L/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.4</td>
<td>19.4</td>
<td>0.4</td>
<td>19.4</td>
</tr>
<tr>
<td>2</td>
<td>2.4</td>
<td>14.0</td>
<td>2.7</td>
<td>8.1</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
<td>7.9</td>
<td>1.3</td>
<td>24.2</td>
</tr>
<tr>
<td>5</td>
<td>3.4</td>
<td>18.4</td>
<td>3.1</td>
<td>7.1</td>
</tr>
<tr>
<td>7</td>
<td>3.6</td>
<td>8.5</td>
<td>3.1</td>
<td>7.1</td>
</tr>
<tr>
<td>Mean</td>
<td>2.5</td>
<td>13.6</td>
<td>1.6</td>
<td>14.3</td>
</tr>
<tr>
<td>SD</td>
<td>1.3</td>
<td>5.4</td>
<td>2.3</td>
<td>8.8</td>
</tr>
</tbody>
</table>

*Lower and upper CIs are shown in parentheses. — Denotes an indeterminate boundary for the CI.
quasisteady state in \( V_{\text{max}} \) could be achieved between the third and fifth breaths after a sudden drop in Pn. These breaths were then used to construct multiple pressure-flow relationships from which Pcrit and Rn were estimated in different body positions and sleep stages. Although our methods permitted two estimates of these variables in NREM sleep (supine and lateral recumbent data), it provided REM data in only half our patients.

There are certain limitations of our methods for determining Perit and Rn. These limitations derive from the fact that Pcrit is a variable inferred from linear regression of the pressure-flow relationship. A natural consequence of this fact is that the precision of our estimate is determined by factors influencing the regression analysis itself. The first factor influencing the precision relates to the scatter of the data points around the regression line. When significant scatter exists, we expect the CI to widen substantially. Under these circumstances, we interpret such widening to be a reflection of the biologic variability in the Pcrit over time. Although such variability may be related to changes in sleep stage over time,\(^{13,16}\) such differences would be minimized with our protocol, which shortens the elapsed time required to acquire pressure-flow data.

Another factor influencing the size of the CI around Pcrit relates to the distribution of data points along the regression axes. When few data exist in the low range of pressure and flow (\( V_{\text{max}} \) of 0 to 100 mL/s), the CI around Pcrit would widen substantially, particularly if back-extrapolation of the pressure-flow relationship to the x-axis is required. Although our protocol stipulated that low-flow data be collected for each patient in the present study, the CI was either indeterminate (see patients 1, 2, and 9 in Fig 4) or excessively wide (patient 5) because premature arousals precluded adequate sampling of low-flow data. It is therefore important that Pn be lowered repeatedly into the range associated with near-zero levels of airflow to minimize statistical uncertainty in estimating the Perit. Thus, low-flow data are required to obtain CI around Pcrit, which reflect the underlying biologic variability rather than statistical uncertainty of this estimate.

CIs for Rn, however, are determined by the precision with which the inverse of the slope of the regression equation can be defined. This variable is best estimated when data are collected over a widely dispersed range of Pn. In practice, data should encompass the range of Pn extending from Perit to approximately 6 cm H\(_2\)O above Pcrit. The upper limit of this range corresponds to the “upper airway opening pressure” as described by Issa and Sullivan\(^{13}\) or the “effective CPAP pressure”\(^{2}\) described by Condos et al.\(^{12}\) This upper limit cannot be extended beyond this range because \( V_{\text{max}} \) cannot be determined at higher pressures, which abolish inspiratory airflow limitation. In our protocol, a stringent criterion for establishing the presence of airflow limitation was also established (see “Materials and Methods”), thereby further reducing the range of Pn over which data were collected. We also constrained the range of Pn applied by adopting a holding pressure equal to the minimum Pn required to eliminate inspiratory airflow limitation. As a result of efforts to standardize the holding pressure and constrain the distribution of data over the Pn range, our CIs for Rn are relatively large, suggesting that our method for estimating Rn is somewhat less precise than that for Pcrit.

Our estimates of upper airway critical pressures during NREM sleep are consistent with those previously generated for the supine condition in NREM sleep.\(^{2}\) Specifically, our Pcrit of 1.8 ± 1.5 cm H\(_2\)O was nearly identical to previous estimates by us of 2.5 ± 1.5 cm H\(_2\)O (Gleadhill et al)\(^{2}\) and others 2.1 ± 0.1 cm H\(_2\)O.\(^{16}\) Of note, the earlier estimates were derived from pressure-flow relationships generated during prolonged periods of sleep at various levels of Pn. The fact that our results with an abbreviated method compare favorably to those obtained with a steady-state method suggests that our method accurately characterizes upper airway collapsibility in apneic patients during sleep. We recognize, however, that reflex responses may alter results obtained from this abbreviated method,\(^{17}\) as evidenced by the increase in \( V_{\text{max}} \) that we detected in the sixth breath after step decreases in Pn in the supine position. The relationship between upper airway neuromuscular activity and Pcrit in sleeping humans, however, is still unclear inasmuch as no differences in Pcrit were detected between NREM and REM sleep despite large differences in genioglossal activity.\(^{7,18}\) Moreover, the two methods have not yet been compared head-to-head, and the accuracy of the newer method is not yet proven in asymptomatic snorers and normal individuals with subatmospheric levels of critical pressure.

With repeated measurements of Pcrit within a single night, we can now examine the sources of variability in upper airway function throughout the night. In the present study, our methods allowed us to discern a statistically significant, albeit modest, decrease in Pcrit between the supine and lateral recumbent positions for a group as a whole. Our findings regarding positional changes are consistent with previous studies\(^{13,19}\) demonstrating a similar direction and magnitude of change in Pcrit. In addition, our methods have allowed us to extend the previous findings in two ways. First, we have established that a lessening in the severity of upper airway obstruction in the lateral recumbent position can be
attributed to alterations in collapsibility (Pcrit) rather than RN. Second, our calculations of CI have now allowed for comparisons of Pcrit within individuals. When CI did not overlap, we took this to indicate that Pcrit decreased significantly in the lateral recumbent position. Thus, our methods have helped to establish the precise mechanism for relief of upper airway obstruction (Pcrit vs RN) in patients with OSA as well as the impact of positional changes on the severity of upper airway obstruction in each patient.

It is perhaps surprising that the RDI did not fall when patients slept in the lateral recumbent position, despite the significant decrease in Pcrit with this maneuver. Although a number of possibilities might account for this finding, we believe that the Pcrit levels in each body position can explain the lack of response in RDI as follows. In previous studies, we observed that little decrease in RDI occurred unless the Pcrit fell below approximately −4 cm H2O.4,5 Indeed, reductions in Pcrit to this level would account for positional responses in RDI in previous reports.21,22 In our patients, however, the supine Pcrit was above atmospheric pressure. With only modest reductions in Pcrit in the lateral recumbent position, Pcrit still exceeded the threshold in all but one patient. With Pcrit remaining only minimally negative, the RDI did not fall significantly. Rather, a shift in the distribution of apneas and hypopneas was found in those patients whose Pcrit fell below atmospheric, consistent with findings from an earlier cross-sectional study in our laboratory.3,5 Thus, it appears that the Pcrit response was too small for the RDI to decrease in our patients, and might be predicted to lower Pcrit sufficiently only in selected patients whose Pcrit is already subatmospheric in the supine position. We would also predict that partial responses in RDI would occur in selected patients in whom the CI overlaps the threshold in the lateral recumbent position. We therefore propose that the Pcrit CI be determined in the lateral recumbent position to target selected patients for positional therapy.6

In summary, our protocol incorporates a number of new features that optimize the estimation of Pcrit and RN from the upper airway pressure-flow relationship. We now believe that rapid, reliable estimates of these variables can be obtained within a single sleep cycle if such a standardized approach is taken to establish both the holding pressure and the range over which the Pn is lowered. Using this protocol, we have also demonstrated the variability in Pcrit related to body position. These latter findings lead us to conclude that better estimates will be obtained when the acquisition of pressure-flow data is restricted to a specific sleep stage and body position. In further studies, our methods may help investigate clinical and physiologic factors influencing the severity of upper airway obstruction during sleep, and may serve to guide clinicians in their selection of therapy for these patients.

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