Mechanical parameters determining pharyngeal collapsibility in patients with sleep apnea

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Obstructive Sleep Apnea is a disorder characterized by pharyngeal collapse and occlusion during sleep. The mechanisms responsible for this disturbance in pharyngeal patency include both anatomic and neuromuscular control factors. Together, these factors render the pharyngeal region to a self-supporting, soft-walled collapsible tube (9, 29), with variable collapsibility. During wakefulness, continuous reflex activation of upper airway dilator muscles maintains adequate pharyngeal patency (20). During sleep and anesthesia, however, these protective mechanisms are deranged, increasing pharyngeal collapsibility and leading to partial or complete occlusions in susceptible subjects.

The mechanical model most commonly used to characterize pharyngeal collapsibility in the nonawake state is the Starling resistor, often served to describe flow mechanics of collapsible biological tubes (9, 26, 29). This simplified model describes an “ideal” collapsible tube that is equivalent to a compliant and collapsible only upstream or nasal pressure (Pn) and the critical collapse pressure (Pcrit) at the pharynx as the variables that define the flow-limiting site (9). This approach is simple and most useful to characterize pharyngeal collapsibility. However, it provides no information about mechanical variables that affect and define the collapsibility of the pharynx. Such variables can be assessed when the flow-limiting site is viewed as a collapsible flow mechanics and pharyngeal collapsibility (critical pressure (Pcrit)). All parameters were measured in 15 patients with obstructive sleep apnea under propofol anesthesia, both at rest and during mandibular advancement and electrical stimulation of the genioglossus. The data was used both to confirm the validity of the model and to compare expected and actual relationships between the tube-law parameters and the pharyngeal pressure-flow relationship and collapsibility. We found a close correlation between predicted and measured Pcrit (R = 0.98), including changes observed during pharyngeal manipulations. C and Ao were closely and directly interrelated (R = 0.93) and did not correlate with Pcrit. A significant correlation was found between Pex and Pcrit (R = 0.77; P < 0.01). We conclude that the pharynx of patients with obstructive sleep apnea can be modeled as an orifice with varying diameter. Pharyngeal compliance and Ao are closely interrelated. Pharyngeal collapsibility depends primarily on the surrounding pressure.

Obstructive sleep apnea is poorly understood. The present study was designed to assess the effects of mechanical properties of the pharynx on airflow. Applying to the pharynx previously published methods to calculate tube-law parameters from the pressure-area relationship of collapsible tubes (28), we measured in anesthetized patients with obstructive sleep apnea mechanical tube-law parameters and flow, and assessed the relative impact of each mechanical parameter on pharyngeal patency and, therefore, on flow limitation and obstruction. To assess the expected effects of the mechanical parameters, we developed a mathematical model to predict the impact of airflow mechanical parameters derived from the pharyngeal tube law on the severity of airflow obstruction. Based on our laboratory’s previous direct observations that the segment of initial (“primary”) pharyngeal collapse appears to be rather short (23), we hypothesized that considerations used to characterize flow and area of a varying orifice, like the aortic valve (7), would also apply to the velopharynx. Measurements were performed under resting, baseline conditions as well as during genioglossus contraction produced by electrical stimulation and during mandibular advancement. The measured parameters and the model predictions enabled us to derive and compare the mechanical parameters most relevant, theoretically (expected by the model) and actually (measured), for pharyngeal flow dynamics and collapsibility.

METHODS

The model. The severity of inspiratory flow limitation is best summarized by the relationship between Vmax and Pn (Vmax:Pn). This relationship describes airflow dynamics through the upper airway between the nose and the pharyngeal site of collapse. To gauge effects of pharyngeal mechanics on flow dynamics, we developed a mathematical approach for modeling airflow dynamics in a collapsible conduit whose primary site of collapse can be modeled as an orifice of
we aimed to maintain the patient under stable anesthesia that eliminated any reaction to pain or to movements of the pharyngoscope, while maintaining adequate ventilation, as monitored by the pneumotachometer and pulse oxymetry.

**Electrical stimulation.** Electrical stimulation of the genioglossus was applied in all patients via Teflon-coated, 0.007-in. diameter hook-wire electrodes with bare ends, inserted sublingually, bilaterally, 10–15 mm deep into the anterior, retro-mandibular body of the genioglossus, as previously described (22–25). Forty-Hertz bursts of 2–6 s, with biphasic pulses of 100-µs width, were applied using a neuromuscular stimulator (Dynex III, Medtronic, Minneapolis, MN). The intensity of stimulation was limited to levels that were well tolerated during wakefulness in previous and preliminary experiments.

**Mandibular advancement.** In seven of the patients, mandibular advancement was performed manually by pulling the mandible anteriorly, with the fingers placed bilaterally behind the rami, to obtain maximal enlargement of the velopharynx, as observed endoscopically (25).

**Experimental procedure.** In addition to conventional polysomnography, patients were prepared with venous access and esophageal balloon, and placed in the supine position. Following induction of anesthesia, $P_n$ was raised to the level above flow limitation that enabled reduction of $P_{ex}$ by at least 2–3 cmH$_2$O without visible reduction in cross-sectional area (holding pressure, range 10–16 cmH$_2$O), the endoscope and genioglossus electrodes were positioned, optimal electrical stimulation characteristics were determined, and the mouth was sealed. The site of collapse was determined visually (pharyngoscope) by gradually lowering $P_n$ and was at the level of the velopharynx in all patients. For data acquisition, the endoscope was placed above the site of collapse with clear visualization of this area, and the tube used to measure intrapharyngeal pressure was placed under vision with the side hole at the level of the site of collapse, facing the lumen. $V_{max}$ and the cross-sectional area of the velopharyngeal site of collapse at multiple $P_n$ levels, before and during electrical stimulation of the genioglossus, were determined simultaneously, as previously described (22, 23). With the patient maintained on holding pressure, $P_n$ was lowered randomly, encompassing 4–10 levels (depending on the pressure range between $P_{ex}$ and $P_{vol}$) associated with inspiratory flow limitation and the level below which

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### Table 1. Anthropomorphic and sleep-study data of patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SE</th>
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</thead>
<tbody>
<tr>
<td>AHI, events/h</td>
<td>36.1 ± 27.7</td>
</tr>
<tr>
<td>Age, yr</td>
<td>46.0 ± 10.0</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>30.4 ± 3.6</td>
</tr>
<tr>
<td>Apnea/tot, %</td>
<td>33.9 ± 33.7</td>
</tr>
<tr>
<td>SO$_2$ &lt; 90%, % (time)</td>
<td>12.9 ± 19.1</td>
</tr>
<tr>
<td>Lowest SO$_2$ (%)</td>
<td>82.9 ± 6.9</td>
</tr>
</tbody>
</table>

Values are means ± SE. AHI, apnea hypopnea index; BMI, body mass index; Apnea/tot, % apneas/total number of apneas + hypopneas; SO$_2$ < 90%, % of sleep time spent with oxygen saturation below 90%; Lowest SO$_2$, lowest oxygen saturation recorded during the sleep study.

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### Fig. 1. Cross-sectional area of the velopharynx (Avp) to intrapharyngeal pressure (Pvp) relationship at the site of pharyngeal collapse in one of the subjects. The curve is exponential, but only the lower, close to linear segment was used to calculate the Avp-Pvp relationship as an estimate of compliance (C) of the site of collapse. The bending point of the Avp-Pvp curve, caused by the transition from high to low C (i.e., from collapse to distension; see *Discussion*), represents the “neutral” area ($A_n$) at which there are no inward or outward elastic wall forces, indicating, therefore, that at this point Pvp is equal to the external pressure ($P_{ex}$).
airflow ceased. At each Pn level, after the fourth breath, genioglossus stimulation was performed for two to three consecutive breaths, and after additional two to three unstimulated breaths, Pn was raised back to the holding pressure, until stable baseline ventilation was observed. After baseline data (averaged from two breaths before and two breaths after genioglossus stimulation) and data during genioglossus stimulation were obtained, mandibular advancement was performed manually and maintained constant, and VImax and velopharyngeal cross-sectional area data were obtained while Pn was lowered repeatedly to multiple levels from the holding pressure.

Data analysis. VImax was measured at the mid-portion of inspiration at each level of Pn, that was associated with flow limitation (as determined from the flow and esophageal pressure tracings). The VImax:Pn curve, known to describe a linear relationship (9, 29), was determined from the flow and esophageal pressure tracings. The bending point of the exponential velopharyngeal cross-sectional area to intrapharyngeal pressure relationship was used as an estimate of pharyngeal compliance at the site of collapse and was determined for the (almost) constant velopharyngeal cross-sectional area at the site of collapse, which to measure velopharyngeal cross-sectional area constant and as a reference for calculating velopharyngeal cross-sectional area in absolute units. The velopharyngeal cross-sectional area at the site of collapse of each digitized frame was outlined and calculated digitally using computer software. The esophageal pressure tube, marked at regular levels, was used as a landmark, in addition to pharyngeal structures, to keep the level at which to measure velopharyngeal cross-sectional area constant and as a reference for calculating velopharyngeal cross-sectional area in absolute units. The velopharyngeal cross-sectional area to intrapharyngeal-pressure relationship was used as an estimate of pharyngeal compliance at the site of collapse and was determined for the (almost) linear portion of this relationship, over the lower velopharyngeal cross-sectional area range, with least square linear regression, since the Pn range over which flow limitation occurs is always within this range (11, 22). The bending point of the exponential velopharyngeal cross-sectional area to intrapharyngeal pressure relationship (11, 12, 28) was used to define Ao, as the cross-sectional area that separates the high- and low compliance parts of the relationship (Fig. 1) at the crossing point of the two (almost) linear parts on both sides of the curve (27). The intrapharyngeal pressure at which Ao was reached was used as an estimate of Pex (see DISCUSSION).

The effect of genioglossus stimulation and mandibular advancement on variables was defined as the difference between the baseline value and the value during manipulation (for example, ΔPcrit during genioglossus stimulation defines the effect of genioglossus stimulation on Pcrit). SPSS was used for statistical analysis. Variables were expressed as means ± SD. To compare calculated and measured data as well as changes in variables during manipulations, we used paired t-test. Multiple regression analysis was used to assess the relationship between tube-law parameters and Pcrit as well as changes in parameters and ΔPcrit during manipulations. P < 0.05 was considered significant.

RESULTS

Model validation. The baseline VImax:Pn slopes and Pcrit values calculated by the model were 3.46 ± 1.48 l·min⁻¹·cmH2O⁻¹ and 1.9 ± 2.8 cmH2O, respectively. To test the validity of our model (see APPENDIX), the individual model-predicted VImax:Pn slope and Pcrit were compared with the

<table>
<thead>
<tr>
<th>Flow − Pressure</th>
<th>Tube-Law Parameters</th>
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<tbody>
<tr>
<td>Pcrit, cmH2O</td>
<td>VImax/Pn, l/min/cmH2O</td>
</tr>
<tr>
<td>BL (n = 15)</td>
<td>1.7 ± 2.9</td>
</tr>
<tr>
<td>ES (n = 15)</td>
<td>−0.3 ± 3.5*</td>
</tr>
<tr>
<td>MA (n = 7)</td>
<td>−2.1 ± 1.7*</td>
</tr>
</tbody>
</table>

Values are means ± SD. BL, baseline; ES, electrical stimulation of the genioglossus; MA, mandibular advancement; Pcrit, critical pressure; VImax, maximal inspiratory flow during flow limitation; Pn, nasal pressure; Rpr, resistance proximal to the site of collapse; Ao, “neutral” cross-sectional area at the site of collapse; Pex, external pressure at the site of collapse. *Significant difference compared with BL (P < 0.001; MA data was compared with BL data of the same patients).
measured values, both baseline data and data during genioglossus stimulation and mandibular advancement. The measured mean data for all patients are given in Table 2. Figure 2 depicts the relationships between measured and predicted values. A high correlation was found for the slope of the $V_{\text{Imax}}:P_n$ curve ($R = 0.89$) and particularly for the $P_{\text{crit}}$ ($R = 0.98$). Similarly, the model closely predicted the magnitude of change in $P_{\text{crit}}$ expected with genioglossus stimulation and mandibular advancement ($R = 0.96$ for the comparison of measured and calculated $\Delta P_{\text{crit}}$ of both values).

**Expected and observed effect of parameters.** Figure 3 depicts the expected effects of changes in $A_o$, C, $R_p$, and $P_{ex}$ on the $V_{\text{Imax}}:P_n$ slope and $P_{\text{crit}}$ calculated with our model. Each part of the figure depicts changes in one of the parameters, with the other three kept constant. To assess the expected effect of these parameters over a wide physiological range, we calculated with the model the $V_{\text{Imax}}:P_n$ for the mean values of the tube-law parameters of our patients (Fig. 3), and each part of the figure evaluated the effect of one of the parameters by calculating the $V_{\text{Imax}}:P_n$ also for the mean $\pm$ SD value of the specific parameter. It can be seen that the four parameters are expected to exert distinct effects: increasing $A_o$ and lowering $P_{ex}$ stabilize the pharynx by lowering $P_{\text{crit}}$ without affecting the $V_{\text{Imax}}:P_n$ slope. Lowering C lowers $P_{\text{crit}}$ but also decreases the $V_{\text{Imax}}:P_n$ slope. Changes in $R_p$ affect only the $V_{\text{Imax}}:P_n$ slope, with $P_{\text{crit}}$ remaining unchanged.

Evaluation of the effects of the measured parameters in our patients on their measured $V_{\text{Imax}}:P_n$ and $P_{\text{crit}}$ revealed, however, that neither C nor $A_o$ correlated significantly with $P_{\text{crit}}$ ($R = 0.09$ and $R = 0.18$, respectively). The absence of this expected relationship was due to a significant interrelationship between C and $A_o$ ($R = 0.93$), since subjects with high $A_o$ tended to have also higher C, both at baseline and after variables were modified by genioglossus stimulation or mandibular advancement ($R$ for $\Delta C$: $\Delta A_o$ during genioglossus stimulation and mandibular advancement $= 0.88$). As shown in Table 2, the significant decrease in $P_{\text{crit}}$ during both genioglossus stimulation and mandibular advancement were not associated with corresponding changes in C and $A_o$, which changed variably and insignificantly with both manipulations. On the other hand, both manipulations decreased $P_{ex}$ significantly. As shown in Fig. 4, $P_{\text{crit}}$ before and during genioglossus stimulation and mandibular advancement, as well as $\Delta P_{\text{crit}}$ with these manipulations, correlate with $P_{ex}$ and $\Delta P_{ex}$ ($R = 0.77$ and $R = 0.72$, respectively; $P < 0.01$ for both), suggesting that $P_{ex}$ is the main variable affecting velopharyngeal collapsibility. The slope of the $V_{\text{Imax}}:P_n$ curve of the patients correlated with $R_p$ ($R = -0.80$; $P < 0.01$), and was not affected by genioglossus stimulation or mandibular advancement.

**DISCUSSION**

In the present study, we developed a mathematical model that relates pharyngeal tube-law parameters and airflow based on basic concepts of aeronautics, describing the pharynx as a variable orifice. We then validated the model by comparing predicted to measured $V_{\text{Imax}}:P_n$ and $P_{\text{crit}}$ in a group of patients with obstructive sleep apnea, thereby confirming the validity of the model and its concepts. Subsequently, we characterized, using the model, the expected effects of tube-law parameters on pharyngeal collapsibility ($P_{\text{crit}}$) and explored the actual interrelationships between these variables and the measured $P_{\text{crit}}$ in our patients. We found that C and $A_o$ are closely interrelated and had no significant correlation with $P_{\text{crit}}$. The peripheral $P_{ex}$ appears to be the principal determinant of pharyngeal collapsibility.

The most commonly used concept to model pharyngeal flow mechanics is the Starling resistor that considers the collapsible segment of the pharynx to represent a self-supporting, soft-walled collapsible tube (9, 29). The collapsibility of such tubes is characterized by the intraluminal pressure that causes the tube to collapse (9, 26, 29). Although easy to use and most useful to quantify pharyngeal collapsibility, it provides no additional information needed to characterize the mechanical properties that determine the degree of collapsibility. Our velopharyngeal cross-sectional area to intrapharyngeal pres-
obstructive sleep apnea severity both before and during mechanical manipulations enabled us to evaluate the actual impact of these parameters. This comparison revealed that, in our patients, C and $A_o$ had no significant impact either on the variability between subjects or on the change in $P_{crit}$ during genioglossus stimulation and mandibular advancement. This lack of significant effect occurred because these two variables tended to cancel each other out: Low C and high $A_o$ prevent collapse, but we found that subjects with low C tended to have low $A_o$ and vice versa, and this reciprocal interdependence prevented a consistent effect of these variables. The cause for this tight linkage between C and $A_o$ could not be derived from our data and is likely to depend on characteristics of tissues surrounding the collapsible site of the pharynx. One may speculate that the frequent failure of palate radiofrequency ablation or implants, expected to lower compliance to improve obstructive sleep apnea (1, 30), may be caused by a concomitant decrease in $A_o$. Interestingly, although dilator muscle contraction would be expected to stiffen the pharynx and reduce its compliance, velopharyngeal compliance was not affected by electrical stimulation of various muscles surrounding the pharynx both in animals and in humans (2, 6, 13, 19) or by mandibular advancement (17). The lack of effect of Rpr on $P_{crit}$ has been shown previously (5), confirming the predictions of our model and the lack of relationships between Rpr and $P_{crit}$ in our patients. It should be noted, however, that Rpr, like the $V_{Imax}$-$P_n$ slope, affects the degree of flow limitation at atmospheric pressure in patients with negative $P_{crit}$ and, therefore, the susceptibility to the development of obstructive hypopneas. The remaining variable, $P_{ex}$, appears to exert the major effect on $P_{crit}$, explaining about half of the interindividual variability and changes observed during manipulations. This conclusion is consistent with recent findings based on directly measured $P_{ex}$ in animal model (14–16).

**Limitations**

We assumed Rps and $P_{ex}$ to be stable over the range of $P_n$ used in this study. Rps represents a similar parameter to $P_n$-$V_{Imax}$-terming upstream resistance and previously shown to be linear (9, 29), indicating stable proximal resistance over the range of flow limitation. Similarly, basic flow conditions were assumed that did not need the more elaborate mathematical tools used to analyze expiratory flow limitation in the lung (18). Although $P_n$-induced changes in pharyngeal size and lung volume could affect $P_{ex}$, its actual effect is difficult to predict (14). The close relationship between the predicted and measured $P_{crit}$ suggests that changes in $P_n$, if present, had a relatively small effect on $P_{ex}$. It should be noted that $P_{ex}$ was not measured but estimated from the velopharyngeal area-pressure curve. Although it may be considered less accurate than a direct measurement, it has the crucial advantage of providing an estimate of the $P_{ex}$ relevant to the specific site of collapse. This parameter is unlikely to be obtainable by direct measurement, since $P_{ex}$ is not evenly distributed along and around the pharynx (14). For this reason, for example, Kairaitis et al. failed to observe decreases in $P_{ex}$ during GG-ES in rabbits but concluded that such reduction must have occurred and could not be demonstrated due to a limitation with the direct measurement of tissue pressure (16). Compliance was calculated in our study from the almost-linear part of the velophar-
ryngal area-pressure relationship over the range of lower Pn relevant for flow limitation (11), a commonly used approach (2, 6, 13, 19). An obvious limitation is that all parameters were determined in anesthetized patients to enable all the measurements and manipulations performed in this study. Although this methodology limits the relevance of our findings to a state of substantial relaxation, the theoretical considerations are the same for relaxed, stable sleep, and propofol seems to have no direct effect on skeletal muscles (8, 21). All our patients had the primary site of collapse at the velopharynx, as indicated by the simultaneous visible pharyngeal occlusion and cessation of flow observed also in our larger study conducted under propofol anesthesia (22). Although there is no obvious reason why our findings should differ in patients with primary oropharyngeal site of occlusion, this condition was not evaluated in the present study. Although the possibility of simultaneous velo- and oropharyngeal occlusion was not excluded in our patients, we have previously found that the oropharynx has a substantially larger cross-sectional area to intrapharyngeal pressure relationship (23). Therefore, even when bi-level collapse occurs simultaneously, small increases in intrapharyngeal pressure above Pcrit enlarge the oropharynx more than the velopharynx, leaving the latter as the flow-limiting site. It should be noted that the model, as presented in this paper, is likely to have primarily a theoretical rather than a practical value, since flow and Pcrit are easier to determine than the tube-law parameters. However, further development of the equations in a way that enables entering the flow-mechanical variables may provide a method to estimate difficult-to-measure tube-law parameters like Pex. Other recently published models using imaging (4, 10) may also obtain practical relevance, if validated.

In conclusion, we developed a mathematical model and confirmed its validity by direct measurements in patients with obstructive sleep apnea. Our findings suggest that changes in pharyngeal compliance are associated with reciprocal changes in Ao that tend to cancel their potential flow-mechanical benefit. Pex was found to be the main determinant of pharyngeal collapsibility. Our findings suggest that manipulations intended to improve pharyngeal patency should try to untie the deleterious linkage between C and Ao and/or aim to reduce Pex.

**APPENDIX**

**Modeling the Relationships Between Pharyngeal Biomechanics and Inspiratory Flow Limitation**

Our approach to modeling upper airway function in the flow-limited condition is based on principles of flow dynamics through a critically restricted orifice. The flow-limiting site can be modeled as a collapsible orifice, whose compliance and external pressure influence its patency, as described by the tube law (area vs. transmural pressure). These components constitute our model system, as depicted in Fig. 5. The model employs three algebraic equations to describe flow limitation in a collapsible tube with a variable orifice. The first equation describes the flow-pressure relationship over the upstream segment into the flow-limited site; the second equation describes flow in a narrow tapering orifice; the third equation describes the tube-law relationship between the cross-sectional area at the flow-limiting site (“choke” point) and the transmural pressure across its wall.

![Fig. 5. The model concepts, considering the site of collapse as a valve-like orifice of varying size. Pvp, intrapharyngeal pressure at the site of collapse in the velopharynx; Pdst, downstream pressure. See text for explanation.](image)

![Fig. 6. Acquisition of the calculated V˙Imax:Pn relationship for one of the patients by the model. After entering the patient’s C, Pex, Ao, and Rpr values, the software calculates for each Pn level the expected flow over a range of Pn levels, when Pdst (the pressure distal to the site of collapse) is reduced gradually (starting with Pdst = Pn). By lowering Pdst (i.e., increasing Pn – Pdst), flow increases until a maximal value is reached (V˙Imax). A further decrease in Pdst results in decreasing flow rates. Plotting all V˙Imax values against the Pn levels at which they were obtained produces the V˙Imax:Pn relationship, and the intercept of this slope with the x-axis provides the calculated Pcrit.](image)
Upstream airway proximal to the collapsing zone. We assume that a modified Bernoulli equation can be written to describe flow dynamics through the upstream and collapsible segments of the upper airway. This equation provides for the preservation of mechanical energy in the air flowing from the entrance to the upstream segment through the nasal passages, to the collapsible site in the pharynx, where linear velocities increase as air is accelerated through the critical orifice. This equation is modified to include a term to account for viscous dissipation of pressure across the resistance proximal to the flow-limiting site.

\[ P_n - P_{vp} = \frac{\rho}{2}(v_n^2 - v_p^2) + R_p V = \frac{\rho}{2}V^2(A_{vp} - A_n^2) + R_p V \quad (I) \]

In this equation, \( P \), \( v \), and \( \rho \) represent the static pressure, average velocity, and density, respectively, and \( R_p \) is the “linear” flow resistance of the upper airway proximal to the site of collapse. \( P_{vp} \) is the intraluminal pressure at the site of collapse (that was at the level of the velopharynx in all our patients), \( V \) is the flow rate (\( V = 4V \)), and \( A \) is the cross-sectional area. Air is considered incompressible in this process since density changes that are associated with pressure changes of about 10 cmH2O or 0.01 atm are negligible.

Downstream orifice segment. The site of collapse is represented by a variable orifice, which tapers and widens along its length. Mechanical energy is lost primarily downstream from the critical orifice where the airway widens once again. Energy dissipates due to the development of vortices and gas separation across this downstream segment, which differs from the viscous laminar flow resistance described in Eq. 1. It is common to assume that pressure in these downstream vortices tends to equalize laterally over the entire cross-sectional area of the downstream segment (7). Under these circumstances, the integral momentum equation relates the pressure difference associated with the deceleration of gas flowing from a narrowed critical orifice into a wide downstream segment. The pressure difference acting across the downstream cross-sectional area produces a force that leads to a change in the velocity of a mass of air as it flows through the downstream segment per unit time (see Eq. 2). Incorporating these principles, we write in the integral momentum conservation to describe the acceleration of air in the downstream segment as follows.

\[ (P_{vp} - P_{dst})A_{dst} = \rho V_{dst}^2 A_{dst} - \rho V_{vp}^2 A_{vp} \rightarrow \]

\[ P_{vp} - P_{dst} = \rho V^2 \left( \frac{1}{A_{dst}} - \frac{1}{A_{dst} A_{vp}} \right) \quad (2) \]

Note that the integral momentum equation is a variation of Newton’s second law: force = mass-acceleration (F = ma, where \( a = dv/dr \) is the derivative of velocity), viz., \( dv/dr \). Substituting \( dv/dr \), we find that \( F = (mdv/dr) \) or \( (md/dr)-dv \). In modeling fluid flow through a conduit, we consider \( md/dr \) to represent the flow rate that enters or leaves a given cross-sectional slice or control volume, whereas \( dv/dr \) represents the difference in velocity between the inflow and outflow of this segment. In other words, a certain mass undergoes a change of velocity as it passes through a control volume within a given time. Its acceleration equals the difference of the \( (md/dr)-dv \) product from the inflow to the outflow (Eq. 2) of this volume. The force that is required to accelerate this mass can be represented by differences in pressure \( \times \) area between the inflow and outflow (Eq. 2). In fluid mechanics, \( (md/dr)-dv \) is the definition of the momentum rate, which is computed or integrated over the entire envelope of the control volume or downstream segment; hence, the equation is called the integral momentum equation, where the terms for force and acceleration are vectors rather than scalars.

The tube law of pharyngeal orifice. Our measured data for the velopharyngeal cross-sectional area \( (A_{vp}) \) vs. the velopharyngeal intraluminal pressure \( (P_{vp}) \) at the site of collapse has a typical format of a three segment function, depending on the pharyngeal pressure range. These functions correspond to specific segments of the cross-sectional area vs. pressure relationship in regions of low compliance, high compliance, and airway closure:

1. \[ A_{vp} - A_0 = (P_{vp} - P_{ex}) C_{vp} \] for \( P_{vp} \geq P_{ex} \)
2. \[ A_{vp} = (P_{vp} - P_{cls}) C = A_0 \frac{(P_{ex} - P_{cls})}{(P_{cls} - P_{ex})} \] for \( P_{cls} < P_{vp} < P_{ex} \)
3. \[ A_{vp} = 0 \] for \( P_{vp} \leq P_{cls} \]

In these equations, \( A_0 \) is the “neutral” cross-sectional area of the velopharynx, when \( P_{cls} = P_{vp} \). Compliances are represented by \( J \) \( (C^* \ll C) \) in the uppermost, low-compliance region and \( 2 \) \( C \) in the high-compliance region of the collapsing velopharynx. \( P_{cls} \) (the pressure at which the site of collapse closes) is \( P_{vp} \) when \( A_{vp} \) reaches zero.

Composite model. The two flow equations (Eqs. 1 and 2), together with the mechanical equation describing the pharyngeal tube law (Eq. 3) were utilized to determine the expected levels of maximal inspiratory airflow over a wide range of upstream (nasal) pressures through the orifice-like pharyngeal site of collapse. These equations were solved simultaneously using a customized algorithm developed for the MatLab Software environment by applying the measured values of \( C \), \( A_0 \), and \( P_{cls} \) from data obtained for each patient from the velopharyngeal cross-sectional area to intrapharyngeal pressure relationship of the site of collapse, and \( R_p \). At any given level of upstream (nasal) pressure \( (P_n) \), inspiratory airflow was computed as the downstream pressure was systematically lowered in ramp-like fashion, producing flow \( \rho_n - \rho_{dst} \) curves. This way, a family of flow-pressure relationships was generated at 0.5-cmH2O \( P_n \) intervals (Fig. 6). Simulating single inspirations for a patient, the model predicts that the flow rate increases, for any given \( P_n > P_{ex} \), with decreasing \( P_{dst} \), until a maximal value is reached \( (V_{max}) \). As shown in Fig. 6, flow limitation is reached, since further decrease in \( P_{dst} \) fails to increase the flow for any given \( P_n \); and with lower \( P_{dst} \) values, the flow rates can even decline. Note that raising \( P_n \) increases \( V_{max} \) and constructing a family of flow \( (P_n - P_{dst}) \) curves over a range of \( P_n \) levels provides a range of \( V_{max} \) levels. Connecting all \( V_{max} \) values provides the \( V_{max} \) relationships of the model (Fig. 6). Interestingly, we found that, using either the data of our patients or theoretical data within the physiological range, the \( V_{max} \) curve was linear. The \( V_{max} \) relationship was generated and fit with least squares linear regression. This relationship was used to solve for \( P_{ex} \) (\( P_n \) at zero flow) and the upstream resistance \( (1/slope) \), providing the model’s predictions of the two major determinants of flow limitation.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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