Measurement of pharyngeal cross-sectional area by finite element analysis

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Mansour, Khaled F., James A. Rowley, and M. Safwan Badr. Measurement of pharyngeal cross-sectional area by finite element analysis. J Appl Physiol 100: 294–303, 2006. First published September 8, 2005; doi:10.1152/japplphysiol.00364.2005.—A noninvasive measurement of pharyngeal cross-sectional area (CSA) during sleep would be advantageous for research studies. We hypothesized that CSA could be calculated from the measured pharyngeal pressure and flow by finite element analysis (FEA). The retropalatal airway was visualized by using a fiber-optic scope to obtain the measured CSA (mCSA). Flow was measured with a pneumotachometer, and pharyngeal pressure was measured with a pressure catheter at the palatal rim. FEA was performed as follows: by using a three-dimensional image of the upper airway, a mesh of finite elements was created. Specialized software was used to allow the simultaneous calculation of velocity and area for each element by using the measured pressure and flow. In the development phase, 677 simultaneous measurements of CSA, pressure, and flow from one subject during non-rapid eye movement (NREM) and rapid eye movement (REM) sleep were entered into the software to determine a series of equations, based on the continuity and momentum equations, that could calculate the CSA (cCSA). In the validation phase, the final equations were used to calculate the CSA from 1,767 simultaneous measurements of pressure and flow obtained during wakefulness, NREM, and REM sleep from 14 subjects. In both phases, mCSA and cCSA were compared by Bland-Altman analysis. For development breaths, the mean difference between mCSA and cCSA was 0.0 mm² (95% CI, −0.1, 0.1 mm²). For NREM validation breaths, the mean difference between mCSA and cCSA was 1.1 mm² (95% CI 1.3, 1.5 mm²). Pharyngeal CSA can be accurately calculated from measured pharyngeal pressure and flow by FEA.

nasopharynx; upper airway; sleep

UPPER AIRWAY CROSS-SECTIONAL AREA (CSA) is a frequently made measurement by researchers investigating upper airway mechanics and pathophysiology. The CSA is measured both to compare baseline mechanical characteristics between groups [such as gender or apnea groups (5, 18, 35, 42)] or to calculate upper airway compliance (Cua) (16, 17, 35, 36). CSA has been measured by a variety of techniques, including nasopharyngoscopy (16–18, 35, 36), acoustic reflectance (26, 27), computerized tomography (42), and magnetic resonance imaging (43). Although all these techniques can be used to accurately measure CSA, disadvantages include an invasive nature for some and either difficult or problematic use during sleep. Therefore, an alternative technique for measuring CSA would be advantageous to upper airway research.

Finite element analysis (FEA) is a computer-based numerical technique used in engineering to calculate the strength and behavior of structures. FEA is a numerical solution to a complex physical problem. The structure of interest is broken down into smaller blocks or “elements.” The behavior of each element can be described with a set of equations. Equations from each element are joined into a large set of simultaneous equations that a computer can solve to describe the behavior of the whole. FEA has been applied to other biological systems, including the upper airway (19). We hypothesized that we could use FEA to calculate the CSA of the nasopharyngeal upper airway. This work describes the development and validation of a FEA model of the upper airway that calculates the nasopharyngeal CSA by using the pressure measured at the nasopharynx and flow measured at the nose, both commonly measured parameters in research of upper airway mechanics.

METHODS

The present study was performed in two stages and was based on previous work from our laboratory. Specifically, we used data on manually measured CSA from a large database of subjects who had participated in two studies of nasopharyngeal imaging previously performed in our laboratory (35, 36). All subjects were free of disordered breathing, including inspiratory flow limitation. Nasopharyngeal CSA data from one subject were used in a development stage; in this stage, the FEA model and equations were developed. In the second stage, we validated the model and equations using data from an additional 14 subjects. Details of the manual determination of CSA and the specific steps performed in the development and validation stages are presented below.

Manual Determination of CSA

The manual determination of CSA using a fiber-optic bronchoscope has been previously described in detail (34–36). The following is a brief summary. Note that the results of the manually determined CSA have been previously reported (35, 36).

Measurements. Electroencephalograms (EEG), electrooculograms (EOG), and chin electromyograms (EMG) were recorded (model 7-B, Grass) using the international 10–20 system of electrode placement (EEG: C3–A2 and C4–A1; EOG F7–A2 and F8–A2). Airflow was measured by a pneumotachometer (model 3700A, Hans Rudolph) attached to a nasal mask. Airway pressure was measured using a pressure-tipped catheter (model TC-500XG, Millar), which was threaded though the mask. By using the fiber-optic scope, the pressure catheter tip was positioned at the level of the retropalatal rim to measure pharyngeal pressure (Pph). Sleep stage was scored according to standard methods (32).

The retropalatal lumen was visualized with a pediatric fiber-optic bronchoscope (FB10X, Pentax). The position of the scope was standardized across subjects by advancing the tip to touch the end of the soft palate and then withdrawing it 2–3 cm. Placement of the endoscope and pharyngeal catheter was performed by one investigator for all subjects (J. A. Rowley). A continuous image of the retropalatal lumen was obtained from a closed-circuit video camera (Endovision 3000, Pentax Precision Instrument) connected to the scope. The video
image and the respiratory signals were digitized at 5 frames/s and 25 Hz, respectively, by using specially developed software. Therefore, for each digitized video image frame, there is a simultaneously recorded time (relative to the beginning of the recording), flow, and Pph.

**Data analysis.** Breaths for analysis were selected during a period of time in which there was no arousal from sleep or any increase in EEG frequency and during which the retropalatal lumen was clearly visible. The retropalatal CSA was obtained for each digitized image frame (5 frames/s) by manually outlining the retropalatal lumen using computer software (SigmaScan, Jandel). During this process, the investigator was blinded to the phase of respiration. An example of an outlined image is shown in Fig. 1. The reproducibility of this technique has been previously validated by our laboratory (47). For each image, the scanning software provided an area in pixels. We converted these relative areas to absolute areas by using the dimensions of the pressure catheter as a reference (21).

**FEA Software**

The simulations were performed by using a commercially available FEA software, Fluid Dynamic International Analyses Package (FIDAP, Fluent, Lebanon, NH). The package includes software to create the mesh from computer-aided design (CAD). The software includes all the equations (including continuity, Navier-Stokes, and mass continuity) to solve for velocity, flow, pressure, and CSA over each element. Finally, it allows the user to solve the complex matrix equations required to calculate the CSA from variables derived for each element of the mesh.

**Development of the FEA Model**

Using coronal and sagittal sections from a magnetic resonance imaging study of the upper airway of one subject (courtesy of Richard Schwab, MD, University of Pennsylvania), we created a three-dimensional model of the upper airway geometry; this model is referred to as the CAD. The CAD created included structures from the nasal inlet to the hypopharynx; however, structures below the level of the nasopharynx (soft palate) were not considered in the equation development because the measurement of CSA and Pph were made at the level of the nasopharynx. A mesh was created from the CAD by first dividing the CAD into 16 sections. Each section is then divided into 10,000 elements [for a total of 160,000 elements; see Fig. 2 (note that the representative CAD shows fewer elements for clarity)]. For the purposes of our model, an element is a small cube at which the analysis will determine the pressure, flow, and velocity.

Certain assumptions are inherent in the development of a FEA model. We considered a streamline of air between two anatomic landmarks: in our case, the nasal inlet and nasopharynx at the level of the edge of the soft palate. At each element between these landmarks, there is a density (ρ), pressure (P), area (A), velocity (U), and flow (F) that characterizes each element. We considered flow both to be incompressible because it has a low velocity and to be quasi-steady (flow into a segment of upper airway will equal flow out of the same segment). We assumed that the flow of air will expand without the loss or gain of heat inside the airway. We assumed that deformation of the CSA will be based on airflow alone. In other words, other potential stresses that might influence CSA, such as caudal traction (49), are ignored at this stage. This is known as a stress-free boundary condition. The boundary conditions will also consist of no-slip (i.e., zero velocity) along all walls. Other assumptions include a fixed upper airway length and that the upper airway wall thickness can be ignored.

Because of the above assumptions, we were able to utilize easily measured parameters such as flow at the nasal entrance, nasopharyngeal pressure, and time of each breath to make subsequent calculations. These measured parameters are considered the boundary conditions or input data. The density of air and airway length (based on the CAD) are also boundary conditions. Therefore, the boundary conditions were the simultaneously measured pressure, flow, and time data points obtained during the initial physiological sleep study. In the initial development stages, the measured CSA (mCSA) that corresponded to the simultaneous measurement of pressure, flow, and time was also included as a boundary condition (see below). During the development stage, we used 677 simultaneous measurements of pressure, flow, and time from 37 breaths obtained from one subject (age 25 yr, body mass index 28.9 kg/m2), without sleep-disordered breathing. Measurements from both non-rapid eye movement (NREM; 341 measurements) and rapid eye movement (REM; 336 measurements) sleep were used in developing the model.

The development of the FEA model is diagrammed in Fig. 3. The boundary conditions are introduced into the mesh. The first objective is to calculate the average viscosity, which is related to the shear forces that influence flow. The shear forces in the upper airway are related to the properties of the upper airway as well as the fluid properties of the airflow. Shear forces will differ between individuals but will also differ between breaths in an individual because shear forces are also related to the velocity and flow, which themselves vary between breaths. To calculate the average viscosity, we first had to measure velocity. Therefore, the previously measured CSA is entered, along with the flow and density into the continuity equation to calculate velocity. The continuity equation is

\[ F = \rho A U \]  

where \( F \) is the flow, \( \rho \) is the air density, \( A \) is the area, and \( U \) is the velocity. \( \rho \), pressure (P), and \( \rho \) are then introduced into the Navier-Stokes equation,

\[ \rho U \frac{\partial U_i}{\partial x_j} = -\frac{\partial P}{\partial x_i} + \mu \frac{\partial^2 U_i}{\partial x_i \partial x_j} \]  

and the mass-continuity equation,

\[ \frac{\partial U_i}{\partial x_i} = 0 \]

Fig. 1. Example of a fiber-optic image of the nasopharyngeal airway with anatomic landmarks identified. Note that the pressure catheter is at the level of the soft palate. The outline of the nasopharyngeal lumen used to calculate the cross-sectional area (CSA) is shown by the white line.
from each combination of simultaneously measured pressure, flow, time, and mCSA. We calculated the average viscosity to be 0.049 N·m/s² (where N is newtons), similar to a value previously reported in the literature (10).

Once the average viscosity is determined, it is entered, along with the pressure, flow, density, and time to measure the resultant velocity by Eqs. 2 and 3. The velocity is then used to determine the calculated CSA (cCSA) using Eq. 1. The average of all the cCSA values (from each combination of simultaneously measured pressure, flow, and time) is then compared with the average of the mCSA values. If the two values are not equal, the number of elements in the mesh is changed (decreased in our model), the boundary conditions are re-introduced, and, by using the average viscosity previously determined, cCSA is determined. Note that in this and subsequent introductions of the boundary conditions the mCSA is not entered. The process is repeated until the mean measured and mean calculated CSA are equal. At this point, the solution becomes mesh independent. In other words, the solution does not depend on the shape of the geometrical airway; it will depend on the simulation equations and the viscosity. For our model, the solution became mesh independent using 8,300 elements.

An example of the results obtained using the FEA method is shown in Fig. 4. Figure 4, top, shows the simultaneous nasopharyngeal pressure and upper airway flow. The output of the FEA model, velocity, and cCSA are shown in Fig. 4, bottom, along with the mCSA. Note that cCSA is similar to mCSA for all images and changes with mCSA throughout the respiratory cycle, indicating the ability of the FEA model to assess dynamic changes in CSA. Note also the large change in CSA throughout the breath, indicating the applicability of the FEA model to a collapsible tube.

Validation of the FEA Model

The FEA model and final equations were validated by using 1,767 simultaneous measurements of pressure, flow, and time from 93 breaths obtained from 14 subjects (8 men, 6 women, mean age 25.8 ± 7.0 yr, mean body mass index 26.2 ± 5.3 kg/m²) during wakefulness (345 images), NREM (415 images), and REM sleep (522 images). None had sleep complaints before study, and none had sleep-disordered breathing during a baseline sleep study. Demographics of each subject and the number of breaths and images used from each subject by stage are shown in Table 1. In choosing subjects, we attempted to have an equal distribution of men and women. In choosing images and breaths, we attempted to have an equal distribution of breaths from each subject from wakefulness and NREM sleep, though we do have increased representation from one subject for NREM sleep. We had fewer subjects to choose from for REM images, which is why there are a larger number of breaths from only five subjects. Most of the subjects had a larger number of breaths and images than analyzed for this study; for uniformity, the first three to four breaths in each subject’s image file were chosen for the validation stage.

Fig. 2. Computer-aided design (CAD) and mesh of the upper airway. The original CAD included all structures from the nasal inlet to the hypopharynx. However, the analysis considered airflow through the nose and nasopharynx (magenta and blue areas) only. White arrow indicates the level at which the CSA was calculated. For clarity, the CAD in the figure shows fewer elements than was used in the model.
During the validation stage, velocity was first calculated by using the average viscosity determined during the development stage, the density, the measurement of pressure and time using Eqs. 2 and 3. The calculated velocity was then entered into Eq. 1 with the flow and density to calculate the CSA. To determine whether the mCSA and cCSA were similar, we performed the following analyses. Bland-Altman analysis was performed using established methods (3). For the development breaths, Bland-Altman analysis was performed on the pooled data and for the data separated by stage of sleep (NREM and REM sleep). For the validation breaths, Bland-Altman analysis was performed on the pooled data and for the data separated by stage of sleep (wakefulness, NREM, and REM sleep). To determine whether the FEA model was capable of assessing dynamic changes in the CSA within a breath, two additional analyses were performed on the validation data. First, for each breath, the images that correlated with four phases of the respiratory cycle were compared. The four phases chosen were beginning inspiration (flow has just become positive), peak inspiratory flow, beginning expiration (flow has just become negative), and peak expiratory flow. Second, we calculated the Cua as previously described (35, 36) for each breath. Compliance was calculated by using both the manually measured CSA (mCua) and the FEA-calculated CSA (cCua), and the two measurements were compared by Bland-Altman analysis.

To explore the reasons for disagreement at higher values of cCSA noted in the validation set (see RESULTS), we also calculated the %error for each image as follows: (mCSA − cCSA) · 100/mCSA.

RESULTS

For the pooled 677 images during the development stage, Bland-Altman analysis revealed a reasonable degree of agreement between the two values with a mean difference of 0.0 mm² (95% CI −0.1, 0.1 mm²), an upper limit of agreement of 21.6 mm² (95% CI 19.2, 24.0 mm²), and a lower limit of agreement of −21.6 mm² (95% CI −24.0, −19.2 mm²). The Bland-Altman analysis for the development stage separated by stage of sleep is shown in Fig. 5. For NREM sleep, the mean difference was 0.6 mm² (95% CI 0.5, 0.7 mm²), an upper limit of agreement of 14.6 mm² (95% CI 12.4, 16.8 mm²), and a lower limit of agreement of −13.4 mm² (95% CI −15.6, −11.2 mm²). For REM sleep, the mean difference was −0.6 mm² (95% CI −0.7, −0.5 mm²), an upper limit of agreement of 26.6 mm² (95% CI 22.2, 31.0 mm²), and a lower limit of agreement of −27.8 mm² (95% CI −32.2, −23.4 mm²).

The results of the Bland-Altman analysis for the validation stage are shown in Fig. 6. For wakefulness (Fig. 6, top), the mean difference between the two values was 1.8 mm² (95% CI 1.7, 1.9 mm²), with an upper limit of agreement of 4.4 mm² (95% CI 4.0, 4.8 mm²) and a lower limit of agreement of −0.8 mm² (95% CI −1.2, 0.4 mm²). For NREM sleep (Fig. 6, middle), the mean difference between the two values was 0.7 mm² (95% CI 0.6, 0.7 mm²), with an upper limit of agreement of 2.5 mm² (95% CI 2.3, 2.7 mm²) and a lower limit of agreement of −1.2 mm² (95% CI −1.4, −1.0 mm²). For REM sleep (Fig. 6, bottom), the mean difference between the two values was 0.9 mm² (95% CI 0.8, 0.9 mm²), with an upper limit of agreement of 1.8 mm² (95% CI 1.7, 1.9 mm²) and a lower limit of agreement of −0.1 mm² (95% CI −0.2, 0.0 mm²). For the pooled group, there was excellent agreement between mCSA and cCSA (data not shown in figure). The mean difference between the two values was 1.1 mm² (95% CI 1.1, 1.1 mm²), with an upper limit of agreement of 3.1 mm² (95% CI 3.0, 3.2 mm²) and a lower limit of agreement of −0.9 mm² (95% CI −1.0, 0.8 mm²).

The Bland-Altman analysis comparing mCSA and cCSA at various portions of the respiratory cycle is presented in Fig. 7. The Bland-Altman analysis showed that the FEA model was accurate at all four points of the respiratory cycle analyzed. Specifically, for the beginning of inspiration (Fig. 7, top left), the mean difference between the two values was 1.1 mm² (95% CI 0.9, 1.3 mm²), with an upper limit of agreement of 3.3 mm² (95% CI 2.6, 4.0 mm²) and a lower limit of agreement of −1.1 mm² (95% CI −1.8, −0.4 mm²). For peak inspiratory flow (Fig. 7, top right) the mean difference between the two values was 1.0 mm² (95% CI 0.8, 1.2 mm²), with an upper limit of agreement of 3.0 mm² (95% CI 2.4, 3.6 mm²) and a lower limit of agreement of −1.0 mm² (95% CI −1.6, −0.4 mm²).
beginning expiration (Fig. 7, bottom left), the mean difference between the two values was 1.1 mm$^2$ (95% CI 0.9, 1.3 mm$^2$), with an upper limit of agreement of 3.3 mm$^2$ (95% CI 2.6, 4.0 mm$^2$) and a lower limit of agreement of $-1.1$ mm$^2$ (95% CI $-1.8$, $-0.4$ mm$^2$). For peak expiratory flow (Fig. 7, bottom right), the mean difference between the two values was 1.1 mm$^2$ (95% CI 0.9, 1.3 mm$^2$), with an upper limit of agreement of 3.3 mm$^2$ (95% CI 2.6, 4.0 mm$^2$) and a lower limit of agreement of $-1.1$ mm$^2$ (95% CI $-1.8$, $-0.4$ mm$^2$).

The Bland-Altman analysis comparing mCua and cCua is presented in Fig. 8. The Bland-Altman analysis showed that the FEA model was accurate for calculating the Cua during wakefulness, NREM sleep and REM sleep. Specifically, for wakefulness (Fig. 8, top), the mean difference between the mCua and cCua was 0.0 mm$^2$/cmH$_2$O (95% CI $-0.4$, $0.4$ mm$^2$/cmH$_2$O), with an upper limit of agreement of 0.4 mm$^2$/cmH$_2$O (95% CI 0.2, 0.6 mm$^2$/cmH$_2$O) and a lower limit of agreement of $-0.4$ mm$^2$/cmH$_2$O (95% CI $-0.8$, $-0.2$ mm$^2$/cmH$_2$O). For NREM sleep (Fig. 8, middle) the mean difference between the two values was 0.1 mm$^2$/cmH$_2$O (95% CI $-0.3$, $0.3$ mm$^2$/cmH$_2$O), with an upper limit of agreement of 0.6 mm$^2$/cmH$_2$O (95% CI 0.3, 0.9 mm$^2$/cmH$_2$O) and a lower limit of agreement of $-0.5$ mm$^2$/cmH$_2$O (95% CI $-0.8$, $-0.2$ mm$^2$/cmH$_2$O). For REM sleep (Fig. 8, bottom), the mean difference between the two values was 0.0 mm$^2$/cmH$_2$O (95% CI $-0.3$, $0.3$ mm$^2$/cmH$_2$O), with an upper limit of agreement of 0.2 mm$^2$/cmH$_2$O (95% CI 0.1, 0.3 mm$^2$/cmH$_2$O) and a lower limit of agreement of $-0.2$ mm$^2$/cmH$_2$O (95% CI $-0.3$, $-0.1$ mm$^2$/cmH$_2$O).

The Bland-Altman plots showed that there was increasing disagreement at larger values of CSA and that there were discrete sets of data. To further analyze this disagreement, we calculated the %error as noted in METHODS. The median %error for all the images was 1.2% (interquartile range 0.14, 1.5%). There was no relationship between the %error and mCSA for the whole group of breaths (Spearman’s coefficient 0.02, $P = 0.40$). Figure 9 shows the median %error for each of the 14 subjects. Median %error ranged from 0.125 to 3.0%. Note that, in eight subjects, the %error was the same for all images analyzed (no error bars are presented), and in the remaining subjects, the variation in the %error was small. Representative data from six subjects demonstrating the relationship between %error and mCSA are shown in Fig. 10. Note that for any given subject the %error is similar across a range of mCSA. Although we chose not to show all subjects for clarity in the figure, a similar relationship between %error and mCSA was seen for all subjects. Therefore, the increased disagreement at

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**Table 1. Subject demographics and distribution of breaths/images**

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<tr>
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<th>Gender</th>
<th>Age, yr</th>
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<th>NREM Breaths/Images</th>
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BMI, body mass index; NREM, non-rapid eye movement sleep; REM, rapid eye movement sleep; M, male; F, female.
larger areas and the presence of discrete sets of data are best explained by intersubject differences in CSA and the %error.

DISCUSSION

In this study, we have demonstrated that FEA can be used to model the upper airway and accurately determine the CSA at the nasopharynx. The CSA calculations were accurate in both wakefulness and sleep and at varying points of the respiratory cycle. In addition, the calculated CSAs could be used to accurately calculate Cua, indicating that the FEA model is capable of assessing dynamic CSA changes. The main requirement for the accurate determination of the nasopharyngeal CSA is a continuous and simultaneous measurement of upper airway flow and Pph.

Methodological Considerations

Several assumptions were made during the modeling process as outlined in METHODS. These assumptions were necessary to allow for the development of the model using standard equations such as the continuity and Navier-Stokes equations. Similar assumptions have been made by another group of investigators who developed a model of airflow through the nasal cavity (19) and are supported by other investigations (11, 14, 31, 40) and the principles of thermodynamics (45). The excellent agreement between the measured and calculated data supports the validity of the assumptions made during the development of the theoretical background. Similarly, we used an average viscosity value calculated by using data from one subject. Differences in shear forces and viscosity values between subjects could explain some of the observed error between subjects.

The FEA model was developed by using one MRI image of an upper airway from just one human subject. Therefore, the mesh developed from the MRI image may not be representative of the normal variation in upper airway anatomy between genders (22, 25), racial groups (8, 33), and individual subjects. In addition, we developed the FEA equations using the measured CSA results from just one subject. We believe that the finding that the degree of error varied by subject is partially explained by intersubject differences in CSA and the %error.
explained by the use of one MRI image and one subject for the development of the model. However, the overall accuracy of the calculated CSA compared with the measured CSA indicates that the final model was mesh independent.

The model was created by using data from subjects without sleep-disordered breathing. Therefore, breaths with inspiratory flow limitation were not specifically analyzed or validated with this model. However, several of the subjects demonstrated large changes in CSA in eupneic breathing (see example in Fig. 4), illustrating that even in normal subjects the upper airway is dynamically collapsing, if not to the point of complete closure. Therefore, we believe that the FEA measurement is applicable to a collapsible tube and capable of measuring dynamic changes in CSA within a short period of time.

The equations for determining pharyngeal CSA were developed by using the previously measured CSA values using a fiber-optic endoscope. Therefore, the measurement of CSA by the FEA model is only as accurate as the original data set. Limitations of fiber-optic endoscopy have been previously discussed (35, 36). The most important consideration is the ability to accurately and reproducibly detect the edge of the airway lumen. Although this process is subjective and operator dependent, we believe that the edge can be visualized with reasonable precision. To ensure this, breaths in which the airway lumen was not clearly visible were rejected for analysis. Previous work has shown that the coefficient of variation is 10% when outlining an image of known diameter, suggesting that changes of less than 20% should be interpreted with caution (47). However, the magnitude of CSA changes seen between stages was greater than this in the majority of patients. Despite these limitations, we believe that the fiber-optic measurements of CSA are reasonably accurate because the values we have obtained compare favorably with those measured by other investigators using fiber-optic endoscopy (with a different measurement technique for CSA) (17), computerized tomography (41), and acoustic reflection (24).

Finally, fiber-optic endoscopy does not allow simultaneous visualization and measurement of CSA at multiple anatomic levels. Previous studies have indicated that the retropalatal airway is the site of maximum narrowing in patients with sleep apnea and normal subjects (13, 18, 29), which is why we originally selected this anatomic level for study. Although we have also measured the CSA of the retroglossal airway (34), we have not yet applied the FEA technique to this anatomic level. If a FEA model for the retroglossal airway could be developed, simultaneous measurement of CSA at two anatomic levels could be performed by using a special pharyngeal catheter that allows pressure measurement at multiple anatomic levels.

Noninvasive Measurement of the Pharyngeal CSA

The CSA of the upper airway has been measured noninvasively by several different modalities; however, none can be considered a “gold standard.” In other words, none of the present methodologies provide an absolute measurement of upper airway CSA against which other methodologies can be compared. Thus comparing the various methodologies to each other is problematic. Radiological imaging procedures, either computerized tomography (7, 20, 30, 41, 42, 44) or MRI (38, 43, 46, 50, 51), are the most common methodologies used to measure CSA. Advantages of radiological imaging include the ability to measure CSA at multiple anatomic levels and to identify structures comprising and surrounding the upper airway, such as the tongue (39), lateral walls (42), and pharyngeal fat pads (51), that may compromise upper airway patency. The
major disadvantage of radiological imaging is the inability to easily perform during sleep, during which the upper airway is most compromised. In addition, the majority of the studies using radiological imaging have not simultaneously measured upper airway pressure and flow. Therefore, although studies using radiological imaging have provided important insights into potential determinants of upper airway patency, it is unclear how the measurements of CSA and upper airway structure relate to changes in ventilation and resistance during eupneic breathing during sleep.

Acoustic reflection has also been utilized by multiple investigators to image the upper airway noninvasively. This technique allows the measurement of CSA at both the nasopharynx and oropharynx (24) and has been utilized to determine the influence of gender (24, 26, 27), body position (24), and lung volume (12) on CSA as well as differences in CSA and airway compliance between subjects with and without sleep-disordered breathing (4, 6). The major disadvantages of this technique are that it must be performed during wakefulness and cannot be used to measure changes in CSA within a breath.

In this study, we have described a unique methodology that allows for the noninvasive measurement of CSA using commonly measured parameters such as flow, nasopharyngeal pressure, and time. The FEA model was developed by using data obtained by nasopharyngoscopy. Nasopharyngoscopy has been utilized by several groups of investigators to measure upper airway CSA during wakefulness (21, 37), anesthesia (16–18), and sleep (2, 28, 29, 34–36). CSAs measured by this technique are approximately the same as those obtained by radiological imaging and acoustic reflectance, indicating that nasopharyngoscopy can provide accurate measurements of CSA. The major advantage of this technique has been the ability to perform imaging studies during sleep, allowing changes in CSA during eupneic breathing to be related to changes in pharyngeal mechanics and resistance. We have

Fig. 8. Bland-Altman analysis for upper airway compliance ($C_\text{UA}$) for individual breaths obtained during wakefulness (top), NREM sleep (middle), and REM sleep (bottom). The plots illustrate that there is excellent agreement between the measured and FEA calculated $C_\text{UA}$, indicating that the FEA model is capable of assessing changes in CSA during the respiratory cycle.

Fig. 9. Box plots of the %error for each of the 14 subjects used in the validation. Note that 8 subjects had the same %error for all images analyzed (subjects with the straight line and circle), whereas the remaining 6 subjects had small variations in %error.

Fig. 10. %Error as a function of mCSA for 6 representative subjects (each represented by one of the 6 symbols seen in the figure). Note that the %error did not vary by mCSA for these 6 subjects; rather, the %CSA was either the same for all images within a subject (○ and ●, △ and ◊) or varied within a subject by stage (● and ○). Although only 6 subjects are represented here, the %error did not vary by mCSA for any subject and for the group as a whole.
shown that finite element analysis can be used to measure the nasopharyngeal CSA with results similar to nasopharyngoscopy. The nasopharyngeal CSA measurement is accurate in both wakefulness and sleep, expanding the applicability of the FEA measurement beyond that of previous noninvasive methodologies, which are limited primarily to wakefulness. In addition, the FEA measurement was able to capture the dynamic changes in upper airway CSA during eupneic breathing, which would allow for measurement of Cua during eupneic breathing.

Disadvantages of the FEA measurement technique relative to other modalities include the following. First, the technique has been validated for measurement of CSA at only one anatomic level, the nasopharynx, limiting the ability to determine changes in CSA at other anatomic levels known to be involved in upper airway patency (29). However, because there are available baseline data for the oropharyngeal CSA, development of a FEA model for the oropharynx is feasible. Second, the technique allows only for the measurement of the CSA of the pharyngeal lumen and does not give insight into other structures of the upper airway that may influence upper airway patency. Third, the technique has only been validated for eupneic breathing. Given that there are likely changes in the properties of the upper airway wall, including shear forces and deformability, during experimental conditions such hypercapnia and hypoxia, this technique cannot be readily used to determine changes in CSA under these conditions.

Implications and Future Directions

The ability to measure CSA noninvasively has both research and clinical implications. We have previously shown that Cua, the change in CSA per unit change in nasopharyngeal pressure, is different between different stages of sleep (36) and genders (35) but have been unable to relate this parameter to other parameters of upper airway mechanics, such as critical closing pressure, or parameters of ventilatory control, such as the apneic threshold, because the invasive nature of nasopharyngoscopy prevents performing intervention studies. With the noninvasive measurement of Cua, we could noninvasively measure Cua during eupneic breathing during wakefulness and sleep and then perform intervention studies, allowing further insights into the influence of Cua on upper airway patency and ventilation. The noninvasive nature of the CSA measurement would also permit its measurement in a larger number and wider variety of patients.

The influence of nasopharyngeal CSA on the type of sleep-disordered breathing event routinely detected on a clinical sleep study is unclear. Although it is commonly accepted that an obstructive apnea represents a complete closure of the upper airway, it is unclear whether hypopnea is associated with upper airway narrowing. Conversely, many normal subjects demonstrated significant airway narrowing without manifesting as "hypopnea" (28, 36). It has been observed that central apneas are associated with airway closure (2). These observations suggest that the magnitude of airway narrowing may not influence the development nonapneic sleep-disordered breathing events; instead, central mechanisms that influence flow and pressure may be more important. Thus FEA may allow for computation of upper airway CSA and provide a robust mechanical corollary for respiratory events.

Alternatively, it is possible that the nasopharyngeal CSA or the degree of narrowing compared with baseline is important to the detection of nonapneic sleep-disordered breathing events. Presently, the clinical detection of these events depends on the measurement of upper airway flow. In particular, the detection of inspiratory flow limitation, essential for the detection of more subtle sleep-disordered breathing events (15), using flow alone can be problematic, with large room for subjectivity (1, 9, 48), although we have recently described a new noninvasive technique that accurately detects inspiratory flow limitation and measures upper airway resistance using only the flow measurement (23). We believe that it may be possible to more accurately detect nonapneic sleep-disordered breathing events by using a combination of flow, upper airway resistance, and nasopharyngeal CSA, all of which can now be measured noninvasively. This may provide an alternative metric to assess the relationship between sleep-disordered breathing and daytime consequences, such as excessive daytime sleepiness and cardiovascular morbidity, particularly in nonapneic forms of the syndrome.

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REFERENCES


