Mechanical properties of the passive pharynx in Vietnamese pot-bellied pigs. I. Statics

STEPHANIE A. TUCK AND JOHN E. REMMERS
Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada T2N 4N1

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First published October 19, 2001; 10.1152/japplphysiol.00761.2001.—The static mechanical properties of the passive pharynx were investigated in Vietnamese pot-bellied pigs by using an isolated upper airway preparation. During general anesthesia and neuromuscular blockade, cross-sectional area (A) of the pharynx was measured while airway pressure (Paw) was held at various pressures in the absence of airflow. The static A-Paw relationship was measured during application of 0, 1, and 2 cm of caudal tracheal displacement. Relative to humans, closing pressures (Pc los e) of the pig pharynx were very low (−15 to −35 cmH2O). Tracheal displacement significantly decreased compliance of the hypopharynx (from 0.074 ± 0.02 cm2/cmH2O with no displacement to 0.052 ± 0.01 cm2/cmH2O with 2 cm of displacement) and decreased Pc los e of the oropharynx (from −18.2 ± 9.9 cmH2O to −24.1 ± 10.5 and −28.7 ± 12.3 cmH2O with 1 and 2 cm of displacement, respectively). Tracheal displacement did not affect A of the pharyngeal segments. In conclusion, tracheal displacement decreased collapsibility of the passive pharynx. The pharynx of the pot-bellied pig is structurally more resistant to collapse than the human pharynx.

caudal tracheal displacement; sleep apnea; pharyngeal compliance; closing pressure

REDUCTION OF PHARYNGEAL DILATOR muscle activity during sleep occurs in normals as well as people with obstructive sleep-disordered breathing (OSDB). However, the sleep-related decrements of pharyngeal dilator activity result in collapse or pronounced narrowing of the pharynx only in the later population. Underlying anatomic abnormalities appear to contribute to narrowing of the pharynx in people with OSDB (6, 10) and, thereby, may play a role in the pathogenesis of OSDB. As neuromuscular activity contributes significantly to airway configuration, distinguishing structural factors relevant to the pathogenesis of OSDB is difficult when neuromuscular activity is present.

A study by Isono et al. (6) investigated the static mechanical properties of the human pharynx in the absence of neuromuscular factors and found differences between normal subjects and patients with obstructive sleep apnea (OSA). They estimated the “tube law” of the pharynx by measuring the relationship between static airway pressure (Paw) and pharyngeal cross-sectional area (A). The authors demonstrated that the pharynx of OSA patients had a smaller maximal area, had a higher closing pressure (the airway pressure at which A = 0; Pc los e), and was more compliant near Pc los e. Thus this study supported the presence of altered pharyngeal mechanics independent of neuromuscular factors in people with OSDB.

Our laboratory has previously described OSDB in obese Vietnamese pot-bellied (VPB) pigs (15). The OSDB in these animals was characterized by high upper airway resistance, snoring, and inspiratory flow limitation associated with marked suppression of genioglossal electromyographic activity but not with obstructive apneas. Thus, under conditions of pharyngeal hypotonia, these animals had a very narrow pharynx but a pharynx that was resistant to complete collapse. We therefore hypothesized that the pharynx of these animals was structurally resistant to collapse.

To shed light on the mechanism of pharyngeal obstruction during sleep in the VPB pig, the first objective of this study was to describe the static mechanical properties of the pharynx in these animals. To test the hypothesis that resistance to complete collapse was an intrinsic mechanical property of the pig pharynx, static mechanics were measured during neuromuscular blockade to eliminate neuromuscular factors. Using an isolated upper airway preparation, we evaluated the static mechanical properties of the passive pharynx by measuring A of the pharynx at various Paw values in the absence of airflow.

The second objective of this study was to investigate the effects of caudal tracheal displacement on the static mechanics of the passive pig pharynx. Studies in feline and canine preparations have indicated that caudal displacement of the trachea decreases collapsibility of the pharynx (9, 14, 17). Because the amount of caudal tracheal displacement varies directly with lung volume (1), changes in lung volume could affect pharyngeal collapsibility through this mechanism. The obese VPB pig exhibits marked braking of expiratory flow, which may be indicative of compromised lung volume (16). Thus reduced end-expiratory lung volume...
in these animals may contribute to increased pharyngeal collapsibility. To test whether caudal tracheal displacement affects pharyngeal mechanics of the VPB pig, we measured static mechanics of the pharynx during varying degrees of tracheal displacement. We hypothesized that increased tracheal displacement would decrease collapsibility of the VPB pig pharynx.

METHODS

Isolated upper airway preparation. Nine mature VPB pigs were studied, six females and three males (2 boars, 1 castrated male). Animal characteristics are shown in Table 1. All protocols were approved by the Animal Care Committee at the University of Calgary. The animal was secured in a supine position with the neck slightly extended. Under general anesthesia (inhaled halothane in 100% O2), the cervical trachea was exposed and transected at the level of the second tracheal cartilage caudal to the cricoid cartilage. The esophagus was ligated at the level of the cricoid cartilage. The femoral artery and vein were catheterized to monitor blood pressure and to administer fluids. The animal was paralyzed throughout the experiment by intravenous administration of pancuronium bromide (0.1 mg/kg every 15 min). Atropine (0.04 ml/kg) was administered intravenously as needed to minimize airway secretions. The nose and mouth of the animal were sealed by using silicone sealant and duct tape.

The caudal cut end of the trachea was cannulated with a cuffed endotracheal tube and attached to a mechanical ventilator in series with an anesthetic machine. The animal was ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The animal was paralyzed and ventilated to maintain an end-tidal PCO2 of 35 Torr. The tracheal cannula in a longitudinal direction with respect to the long axis of the trachea until the caudal edge of the trachea had been displaced either 1 or 2 cm.

Data analysis. At each value of static Paw, three images of the pharyngeal lumen, separated by 100 ms, were analyzed by digitally capturing the pharyngeal images by using frame-grabber software (Snap Magic, Quantum). Each digitized image was displayed by using image-analysis software (SigmaScan, Jandel Scientific), the pharyngeal lumen was traced, and A of the lumen in pixels was calculated. The mean A at each Paw was used for analysis. A was converted to centimeters squared by using a conversion factor based on the distance-magnification relationship of the endoscope (see Endoscope calibration).

A was plotted vs. Paw for each pharyngeal segment and for each condition of tracheal displacement and fit with linear regression. Compliance (dA/dP, where P is airway pressure) was calculated as the slope of the A-Paw relationship. dA/dP was normalized to airway size by dividing by the A of the segment at atmospheric pressure. Pelose was calculated as the Paw at which A = 0. Pelose was extrapolated from the linear regression if necessary.

Endoscope calibration. The distance-magnification relationship of the endoscope was determined by using four circular calibration disks. The endoscope was supported vertically above each disk, and images were collected at 5-mm increments in distance between the disk and endoscope tip from 10 to 35 mm. Images were digitized and A calculated as described above. Calculated A of the disks, expressed as pixels, was plotted against actual A in centimeters squared for each distance between the disk and endoscope tip (endoscope distance) to obtain a conversion factor from pixels to centimeters squared. During experiments, endoscope distance was measured by passing a second catheter into the pharynx.

Statistical analysis. The effects of tracheal displacement on the dependent variables (dA/dP, Pelose, A) were analyzed by using a repeated-measures ANOVA. Tukey’s test was used for post hoc analysis. To determine whether pharyngeal dA/dP or Pelose was related to animal weight or body mass index (BMI), the strength of association between the dependent variables and weight and BMI were determined by Pearson product-moment correlation.

RESULTS

Endoscope calibration. The calculated A values of the disks in pixels were linearly related to actual A values in centimeters squared, but the slope of this relationship varied with endoscope distance according to the relationship: absolute area (cm2) = image area/31,920-0.85 · scope distance. Endoscope distance measurements were not made in three animals because of technical difficulties; therefore, not all pharyngeal A values were expressed in absolute units.

Static A-Paw relationships. In some animals, we were unable to successfully measure the A-Paw rela-

### Table 1. Animal characteristics

<table>
<thead>
<tr>
<th>Pig No.</th>
<th>Sex</th>
<th>Weight, kg</th>
<th>BMI, kg/m²</th>
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<tr>
<td>1</td>
<td>M</td>
<td>36</td>
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<td>M</td>
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<tr>
<td>9</td>
<td>F</td>
<td>100</td>
<td>92</td>
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Mean ± SD 93.8 ± 47.8 92.5 ± 13.5

M, male; F, female. Body mass index (BMI) was calculated as weight (kg)/[ear-to-tail length (m)]².
tionship under all conditions. The majority of the A-Paw relationships were well described by linear regression (mean $r^2 = 0.93$). Five of 64 data sets were poorly fit by linear regression ($r^2 < 0.85$) and were excluded from analysis; two were better fit with a sigmoidal function (mean $r^2 = 0.99$), two with an exponential growth function (mean $r^2 = 0.97$), and one with an exponential rise function ($r^2 = 0.99$). $dA/dP$, $P_{\text{close}}$, and $A$ of the three pharyngeal segments measured at atmospheric pressure are shown in Fig. 1. Mean $dA/dP$ and $P_{\text{close}}$ of the hypopharynx exceeded the nasopharyngeal values ($P < 0.05$). Thus the nasopharynx was a relatively narrow, noncompliant structure difficult to collapse; the hypopharynx was also narrow but significantly more collapsible than the nasopharynx. The oropharynx was large and of intermediate compliance and $P_{\text{close}}$ relative to the other segments.

The A-Paw relationships for each pharyngeal segment at 0, 1, and 2 cm of tracheal displacement for one animal (pig 4) are shown in Fig. 2. The effects of tracheal displacement on $dA/dP$ and $P_{\text{close}}$ of the group are shown in Fig. 3. Although a trend existed for stiffening of the pharyngeal segments with tracheal displacement, the decrease in $dA/dP$ was significant only for the hypopharynx at 2 cm of displacement. Tracheal displacement tended to decrease $P_{\text{close}}$ of the nasopharynx and oropharynx, although only significantly for the oropharynx at both 1 and 2 cm of displacement. Tracheal displacement had little effect on $P_{\text{close}}$ of the hypopharynx.

The change in $A$ of the pharyngeal segments with tracheal displacement is shown in Fig. 4. The change in $A$ with tracheal displacement is shown not only for data sets with $A$ expressed in centimeters squared (Fig. 4A) but also for data sets where endoscope distance measurements were not successful; thus $A$ is expressed in pixels (Fig. 4B). Values of $A$ of the pharyngeal segments at 2 cm of tracheal displacement (whether measured as cm$^2$ or pixels) were not different from resting values (0 cm of displacement) at atmospheric pressure ($P < 0.05$). When Fig. 4A is compared with Fig. 4B, the data suggest a small but consistent trend for enlargement of the nasopharynx with tracheal displacement. For the oropharynx and hypo-
pharynx, however, the direction of change of $A$ with tracheal displacement was not consistent. This inconsistency, with the finding of a lack of statistically significant differences in changes in $A$, supports a conclusion that tracheal displacement had little effect on size of these pharyngeal segments.

Measurement of the strength of association between $P_{\text{close}}$, $dA/dP$, and $A$ and BMI revealed that $A$ of the nasopharynx had a significant positive correlation with BMI ($r^2 = 1.0$, $P < 0.05$). $dA/dP$ and $P_{\text{close}}$ of the pharyngeal segments, however, did not correlate significantly with BMI.

DISCUSSION

We measured the static mechanical properties of the passive VPB pig pharynx and investigated the effects of tracheal displacement on pharyngeal mechanics. The passive pharynx of this animal is characterized by a narrow, collapsible hypopharynx; a relatively large but moderately collapsible oropharynx; and a nasopharynx that was incompliant and difficult to collapse. Compared with humans, the pig pharynx is more resistant to collapse, perhaps contributing to the absence of obstructive apneas during sleep in this animal. Consistent with other studies, tracheal displacement decreased collapsibility, although displacement had differential effects on the various pharyngeal segments.

Although similar isolated upper airway preparations have been developed in other species (3, 11, 14), this is currently the only preparation that uses an animal with documented OSDB. Thus the main advantage of the VPB pig preparation is that the relationship between the mechanical properties of the pharynx and characteristics of OSDB in this animal can be explored.

Methodological issues. Although endoscopy permits direct observation of the pharyngeal lumen at various airway pressures, the technique has several limitations. To compare $A$ between conditions, $A$ must be expressed in absolute units. Two methods previously used to obtain absolute measurements from endoscope images used either covisualization of a structure of known dimensions such as a pressure catheter and the lumen (4, 7) or measurement of the distance between the endoscope and the plane of interest (6). We chose to pass a second catheter into the pharynx to measure the distance between the endoscope tip and the plane of interest. Because of difficulties in visualization of a second catheter within the pharyngeal lumen, endoscope distance measurements were not always successful. This method also assumes that the endoscope distance remains constant during measurements. Although care was taken to minimize endoscope movement, slight changes in endoscope distance may have occurred, potentially adding variability to the calculated $A$. A further limitation of endoscopy is the radial distortion of the image due to the optics of the endoscope, manifest as a progressive reduction in image magnification from the center to the periphery of the endoscope field of view. $A$ measurements were not corrected for radial distortion, although we attempted to center the pharyngeal lumen in the endoscope field of view during image collection.

Static mechanics. Regional differences in the static mechanics of the pharynx were evident. The nasopharynx had more prominent collapsibility than the oropharynx.
The pharyngeal A-Paw relationship of the pigs was well described by a linear function in the pressure range studied, and A did not reach a plateau at the highest value of Paw (>15 cmH2O). This differs from the A-Paw relationship of the passive human pharynx where pharyngeal A was an exponential function of Paw; at Paw <5 cmH2O, the slope of the relationship was quite steep, and A reached a plateau at Paw = 10–15 cmH2O (4, 6). Why the pig pharynx is more compliant at high Paw is unknown. One possible explanation may relate to differences in the tissue pressure (Pti) surrounding the pharynx. The Paw-A relationship of the pharynx, as measured in the present study and the studies of Isono et al. (4, 6), where the difference between Paw and atmospheric pressure is used, reflects the true tube law of the pharynx only if Pti = 0. However, Pti likely has a finite value (5, 20), and, furthermore, it probably varies with pharyngeal airway volume. What determines Pti is unclear, but it is likely related to the properties of the tissues surrounding the pharynx and the compliance of these tissues when displaced. Perhaps differences in the properties of the tissues surrounding the pharynx between humans and pigs contribute to differences in compliance at high Paw.

Values of Pclose of the pig pharynx (−15 to −35 cmH2O) were much lower than reported for humans (−4 to −2 cmH2O) (4, 6). The greater resistance to collapse of the pig pharynx under static conditions may be related to differences in upper airway structure. The retropalatal position of the epiglottis in the pig may inhibit dorsal movement of the free edge of the soft palate or the tongue base toward the posterior pharyngeal wall, common mechanisms of pharyngeal collapse in humans. The structure of the hyoid apparatus may also contribute to differences in Pclose. In humans, the position of the hyoid can affect pharyngeal collapsibility through the actions of muscle inserting on or originating from the hyoid bone (8, 19). The hyoid apparatus of pigs is “strutted” such that the main body of the hyoid is attached to the skull by cartilaginous rods (12). This bony arch support in the pig contrasts with the nonarticulated, “floating” hyoid of humans and may provide additional structural support, independent of neuromuscular activity, to the ventral wall of the pharynx.

The low Pclose values of the pig pharynx likely explain why high upper airway resistance but not obstructive apneas were observed in the obese animals during sleep. If Pclose of the pharynx is less than (i.e., more negative) the negative intraluminal pressure generated during inspiration, occlusion of the pharynx will not occur. Resistance upstream from the pharynx is likely not negligible in the pig; therefore, negative intraluminal pressures generated during inspiration could be substantial. Tracheal pressures often reached −10 cmH2O during spontaneous breathing in the sleeping animal but rarely exceeded −15 cmH2O (unpublished observations). Therefore, intraluminal pressures were rarely more negative than the highest Pclose of the pharynx (−15 cmH2O; hypopharynx) during inspiration. Thus intraluminal pressures generated during inspiration would likely cause significant narrowing of the pharynx and increased upper airway resistance but not complete pharyngeal obstruction. This is in agreement with our observations of high upper airway resistance but no obstructive apneas during sleep in the VPB pig (15).

Because we were interested in the intrinsic mechanical properties of the pharynx, measurements were made during pharyngeal atonia. The presence of pharyngeal dilator activity would likely shift the pharyngeal A-Paw curve to the left and/or decrease dA/dP. Thus suppression of pharyngeal dilator activity from wakefulness to sleep would result in a more compliant and/or narrower pharynx, manifest as increased airflow resistance and inspiratory flow limitation during sleep. Although sleep is often described as a condition of pharyngeal hypotonia, the pig pharynx is not completely devoid of neuromuscular influences during sleep, even rapid eye movement sleep (15). Thus the pharynx of the sleeping animal would likely be less collapsible compared with the paralyzed condition of this study.

Obesity is present in the majority of humans with OSDB and is a major risk factor for development of OSDB (21). Obesity may alter pharyngeal mechanics through loading of the pharynx by subcutaneous fat or by encroachment from fat deposits lateral to the pharynx. Because we studied animals with a wide spectrum of BMI, we were interested as to whether BMI was correlated with static mechanics of the pharynx. A higher BMI was associated with increased nasopharyngeal A, but BMI did not correlate with dA/dP or Pclose of the pharyngeal segments. The relationship between BMI and nasopharyngeal A may be due to the animals with higher BMIs also being larger in general stature. Thus evidence of altered pharyngeal mechanics associated with obesity was not found in these animals.

Effect of tracheal displacement. Caudal traction transmitted to the upper airway is thought to stabilize the pharynx (17, 18). Decreased upper airway resistance (17) and improved airflow dynamics (9, 14) with caudal tracheal displacement have been previously shown in animal studies. The present study further elucidates the effects of caudal tracheal displacement on upper airway mechanics by investigating its effects on discrete segments of the pharynx as opposed to effects on global behaviour of the entire upper airway as measured in previous studies. Also, the effects of
tracheal displacement on pharyngeal size, evaluated by visualization of the pharyngeal lumen, have not been previously reported. The results of the present study agree with previous studies in that increased tracheal displacement is associated with decreased pharyngeal collapsibility (9, 14, 17, 18).

Tracheal displacement and its effects on pharyngeal collapsibility may be important in the pathogenesis of OSDB in the intact VPB pig. The degree of tracheal displacement varies directly with lung volume, contributing to the well-known inverse relationship between lung volume and upper airway resistance (1). The sleeping obese VPB pig exhibits pronounced expiratory traction due to the pull of the descending diaphragm (16). Therefore, reduced caudal tracheal traction due to reduced end-expiratory lung volume may predispose the pharynx to collapse in the obese VPB pig.

In intact humans and animals, changes in caudal traction on the trachea also occur within the breathing cycle; tracheal displacement increases with each inspiration due to the pull of the descending diaphragm transmitted through mediastinal structures and negative swings in intrathoracic pressure (18). On the basis of our findings, caudal tracheal traction during inspiration may stabilize the pharynx in the intact animal by decreasing hypopharyngeal compliance and oropharyngeal closing pressure, making the pharynx less collapsible.

The mechanism by which caudal tracheal displacement decreased collapsibility appeared to vary depending on the pharyngeal segment. The decrease in compliance of the hypopharynx with tracheal displacement may have been due to increased longitudinal tension in the hypopharyngeal walls. Although no studies have examined the length-tension relationship in the pharynx, work in other systems such as isolated trachea suggests that increased longitudinal tension decreases wall compliance (2, 13). Alternately, tracheal displacement may have altered forces acting on the epiglottis through its laryngeal origin. If tracheal displacement increased the distance between the base of the epiglottis and the hyoid apparatus, increased passive tension on the hyoepiglotticus muscle (the equivalent of the hyoepiglottic ligament in humans) may occur. This increased ventral force acting on the epiglottis may contribute to a decreased hypopharyngeal compliance.

Unlike the hypopharynx, tracheal displacement decreased Pclose of the oropharynx but did not affect oropharyngeal compliance; i.e., a leftward shift in the A-Paw relationship occurred. An enlargement of the oropharynx with tracheal displacement could explain this leftward shift; however, A of the oropharynx was not significantly different between 0 and 2 cm of displacement.

In conclusion, the passive VPB pig pharynx is structurally more resistant to collapse than the human pharynx, and the low Pclose of the pig pharynx likely underlies the absence of obstructive apneas in the intact animal during sleep. Caudal tracheal displacement decreased collapsibility of the pharynx by decreasing hypopharyngeal compliance and oropharyngeal Pclose. The VPB pig isolated upper airway preparation provides a useful tool for understanding determinants of pharyngeal patency. Further investigations using this preparation could include the effects of selective stimulation of pharyngeal dilator muscles on dA/dP and Pclose of specific pharyngeal segments to elucidate effects of muscle activation on pharyngeal mechanics.

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REFERENCES