Mechanical effects of pharyngeal constrictor activation on pharyngeal airway function

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Kuna, Samuel T., and Christi R. Vanoye. Mechanical effects of pharyngeal constrictor activation on pharyngeal airway function. J. Appl. Physiol. 86(1): 411–417, 1999.—The mechanical effects of pharyngeal constrictor (PC) muscle activation on pharyngeal airway function were determined in 20 decerebrate, tracheotomized cats. In 10 cats, a high-compliance balloon attached to a pressure transducer was partially inflated to just occlude the pharyngeal airway. During progressive hyperoxic hypercapnia, changes in pharyngeal balloon pressure were directly related to phasic expiratory hyopharyngeus (middle PC) activity. In two separate protocols in 10 additional cats, the following measurements were obtained with and without bilateral electrical stimulation (0.2-ms duration, threshold voltage) of the distal cut end of the vagus nerve’s pharyngeal branch supplying PC motor output: 1) pressure-volume relationships in an isolated, sealed upper airway at a stimulation frequency of 30 Hz and 2) rostrally directed axial force over a stimulation frequency range of 0–40 Hz. Airway compliance determined from the pressure-volume relationships decreased with PC stimulation at and below resting airway volume. Compared with the unstimulated condition, PC stimulation increased airway pressure at airway volumes at and above resting volume. This constrictor effect progressively diminished as airway volume was brought below resting volume. At relatively low airway volumes below resting volume, PC stimulation decreased airway pressure compared with that without stimulation. PC stimulation generated a rostrally directed axial force that was directly related to stimulation frequency. The results indicate that PC activation stiffens the pharyngeal airway, exerting both radial and axial effects. The radial effects are dependent on airway volume: constriction of the airway at relatively high airway volumes, and dilation of the airway at relatively low airway volumes. The results imply that, under certain conditions, PC muscle activation may promote pharyngeal airway patency.

The upper airway is a common conduit for the respiratory, digestive, and phonatory systems. Skeletal muscles surrounding the potentially collapsible pharyngeal airway are required to perform conflicting functions: to maintain airway patency for respiration, to promote airway closure for swallowing, and to valve and shape the airway for phonation. The superior, middle, and inferior pharyngeal constrictor (PC) muscles form the lateral and posterior walls of the pharyngeal airway. PC activation promotes airway closure in the pharyngeal phase of swallowing. However, the PC muscles also exhibit respiratory-related activity; this suggests a role for these muscles in the control of pharyngeal airway function during respiration. Neurophysiological studies report that the nerves supplying motor output to the PC muscles contain fibers which discharge on inspiration and/or expiration (4, 7). Most electromyographic (EMG) studies in animals and humans report that the PCs exhibit phasic activation during expiration, particularly during hypercapnic and hypoxic conditions (2, 3, 9, 11, 12, 15–18, 21, 22). Studies in patients with obstructive sleep apnea (OSA) report phasic PC activation during inspiration, associated with airway reopening at the end of an induced or spontaneous obstructive apnea (8, 14).

Respiratory-related activation of a constrictor muscle surrounding a potentially collapsible airway could conceivably compromise airway patency. Previous investigators have speculated on the effect of respiratory-related PC activation on pharyngeal airway function. Sherrey and Megirian (21) suggested that airway constriction from PC activation under hypercapnic conditions decreases dead space, thus helping to promote elimination of CO₂. Murakami and Kirchner (18) hypothesized that phasic expiratory PC activation serves to return the hyoid and thyroid cartilages to their end-expiratory position after their caudal movement during inspiration. The patterns of respiratory-related PC activation observed during repetitive pharyngeal airway closure during sleep in the OSA patients led to the hypothesis that these muscles may, under certain circumstances, help to protect pharyngeal airway patency by stiffening and dilating the airway (8, 14).

The purpose of the present study was to determine the mechanical effects of PC activation on the pharyngeal airway function and to better understand 1) the potentially conflicting roles of PC activation during swallowing and respiration, and 2) the inspiratory activation of this normally phasic expiratory muscle during airway reopening after an obstructive apnea in OSA subjects. Three protocols were performed in tracheotomized, decerebrate cats. Protocol 1 correlated respiratory-related PC activity with pressure in a high-compliance balloon that occluded the pharyngeal airway during progressive hyperoxic hypercapnia. Protocol 2 determined the pressure-volume relationships in the pharyngeal airway with and without bilateral electrical stimulation of the pharyngeal branch of the vagus nerve supplying motor output to the PC muscles. Protocol 3 measured the rostrally directed axial force generated by bilateral electrical stimulation of the pharyngeal branch of the vagus nerve. The results indicate that PC activation stiffens the pharyngeal airway and has both radial and axial mechanical effects.

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METHODS

Acute experiments were performed in 20 decerebrate, tracheotomized adult cats of either sex weighing 3.0–4.0 kg. Protocol 1 was performed in 10 cats. Protocols 2 and 3 were performed in 10 additional cats. The protocols were approved by the Animal Care Committee of The University of Texas Medical Branch at Galveston.

Anesthesia was induced with halothane. The animals were intubated, and the anesthetic was continued until completion of all surgery. Arterial blood pressure was monitored with a cannula attached to a pressure transducer (Statham) in the femoral artery. A cannula in the femoral vein was used to infuse medications and fluids. Mean blood pressure remained >100 mmHg in all animals. Temperature of the animals was controlled at 37°C with a servo-controlled heating pad (Yellow Springs Instruments). After dexamethasone (3 mg iv) was administered to help control brain edema, an intercollicular decerebration was performed by using the technique of Kirsten and St. John (13). A tracheotomy was performed through a midline ventral neck incision, and cannulas were placed in the rostral and caudal trachea. The animals breathed through the caudal tracheal cannula throughout the recordings. A side arm in the caudal tracheal cannula was used to continuously sample gas for the measurement of end-tidal CO₂ (Datex).

With the use of this surgical exposure, the hypopharyngeal (middle PC) was easily identified as the sheet of muscle in the outer lateral pharyngeal wall between the hyoid bone and rostral rim of the thyroid cartilage.

A pair of 38-G hooked-wire electrodes (Belden) was implanted under direct vision into the hypopharyngeal muscle in all protocols and in the cricothyroid muscle (n = 6) in protocol 1 by using the technique of Basmajian and Dutta (2, 3). Each wire of the electrode pair was implanted separately. The wires were inserted superficially into the thin PC muscles in the lateral pharyngeal wall to avoid the posterior pharyngeal relationship between Pbal and PC activity in the presence of tracheal movement and/or cricothyroid muscle contraction. The EMG signals were amplified, filtered (Grass, Tektronics, respectively), and displayed on an oscilloscope. The cats were studied in the supine position. All data were recorded on a polygraph (Gould) and magnetic tape (Neurocorder). The data were digitized off-line at 500 Hz (RC Electronics) and analyzed by using computer software (Run Technologies).

Protocol 1: Effect of PC activation on pharyngeal balloon pressure (Pbal). In protocol 1, a high-compliance balloon (Mallinckrodt) attached to a pressure transducer (Statham) was inflated in the pharyngeal airway with just enough air to occlude the airway (Fig. 1). A positive pressure in the balloon throughout the respiratory cycle was taken as evidence that the airway was indeed occluded. Progressive hyperoxic hypercapnia was induced by connecting the caudal tracheal cannula to a 1-liter reservoir bag containing 7% CO₂-balanced O₂. At given levels of end-tidal CO₂, the following outcome parameters were determined for five consecutive breaths and expressed as a mean: phasic and tonic muscle activity, maximum Pbal during expiration, and minimum Pbal during inspiration. Results during the rebreathing test were compared by using the Wilcoxon signed rank test to determine the relationship between Pbal and PC activity in the presence and absence of tracheal movement and cricothyroid activation. Comparisons with P < 0.05 were considered statistically significant.

Protocol 2: Effect of PC activation on pressure-volume relationships in the isolated, sealed pharyngeal airway. The isolated, sealed upper airway preparation detailed by Hida et al. (10) was used in protocol 2 to determine the pressure-volume relationship of the pharyngeal airway with and without PC activation. The sealed rostral tracheal cannula was immobilized at resting position with a table-based damp, and the mouth and nose were sealed with a silicone elastomer (Factor II). A ligature was placed around the esophagus at its rostral origin. The superior laryngeal nerve was severed bilaterally. Pressure in the isolated, sealed upper airway was measured from the rostral tracheal cannula and from an oral cannula (Statham) in the mouth. An airtight seal was determined by the absence of drift in airway pressure after the injection or withdrawal of air. The pressure transducers were calibrated with a water manometer.

The animals were mechanically ventilated on a time-cycled ventilator (Harvard Apparatus) to suppress spontaneous respiratory efforts. This was usually achieved at an end-tidal CO₂ of 3.5–4.0%. This passive hyperventilation induced glottic closure (16); therefore, an 8-Fr fenestrated polyethylene tube was advanced through the rostral trachea just past the vocal cords to allow transmission of pressure from the

Fig. 1. Schematic diagram illustrating experimental technique used in protocol 1. Pharyngeal pressure was measured with a high-compliance balloon, attached to a pressure transducer, inflated in the pharyngeal airway with just enough air to occlude the airway.
caudal pharynx to the pressure transducer in the rostral tracheal cannula.

The pharyngeal branch of the vagus nerve was dissected free and was severed bilaterally at its origin from the inferior ganglion of the vagus nerve. Each unsheathed nerve ending was placed on a bipolar stimulating electrode immersed in mineral oil. The nerves were stimulated with pulses of 0.2-ms duration (Grass). Stimulation of the nerve produced visual contraction of the PC muscles and a shock artifact on the hyopharyngeus EMG. The voltage threshold to induce PC contraction at 5-Hz stimulation frequency was determined by visual observation and was used as the voltage intensity throughout the rest of the experiment. The average voltage threshold was 3.0 V. For all trials in protocols 2 and 3, stimulation periods were 10–15 s in duration and separated by at least 2 min. This interval between stimulation periods maintained a consistent pressure response to stimulation under a given condition over the duration of the experiment.

With the isolated, sealed upper airway at its resting volume, stimulation frequency was progressively increased in 5- to 10-Hz increments until there was no change in maximum pharyngeal pressure. The pressure-volume relationship in the isolated, sealed upper airway at volumes above and below resting volume was determined with and without bilateral stimulation of distal cut end of pharyngeal branch of the vagus nerve. P1, P2, pressure transducers 1 and 2, respectively.

The highest and lowest common volumes obtained during all trials in protocols 2 and 3 were tested to generate each pressure-volume relationship. A known volume of air was then injected or withdrawn from the airway. A minimum of eight different volumes were tested to generate each pressure-volume relationship. Trials in which withdrawal of volume was associated with a difference between the two pressure signals were not analyzed, because this pressure discrepancy was felt to indicate the presence of pharyngeal airway closure.

Each pressure-volume relationship was fitted with a third-order regression equation. The regression equation was used to obtain the following data during unstimulated and stimulated conditions: slope (ΔV/ΔP) of the pressure-volume relationship, and change in pressure between the unstimulated and stimulated conditions. These data were obtained at three airway volumes: resting volume, 0.90 ± 0.32 (SD) ml above resting volume (relatively high airway volume), and 1.83 ± 0.35 ml below resting volume (relatively low airway volume). The highest and lowest common volumes obtained during the unstimulated and stimulated conditions were used in each cat. The pressure and volume decrement from the resting volume (where the unstimulated and stimulated pressure-volume curves intersected) was also determined. A repeated-measures ANOVA was used to compare the effect of airway volume, and a paired t-test was used to compare the effect of PC stimulation on the above outcome parameters. Values of P < 0.05 were considered significant.

Protocol 3: Axial effects of pharyngeal constrictor activation. Protocol 3 measured the axial force generated by PC activation. With the exceptions detailed below, the preparation was the same as that in protocol 2. The trachea between the rostral and caudal tracheal cannulas, strap muscles, and esophagus were severed. The freed rostral end of the trachea was attached to a force transducer (Statham) positioned over the sternum. The force exerted without stimulation was sufficient to bring the rostral tracheal cannula to the same position it had before the trachea was severed. The force of PC contraction was progressively increased by increasing stimulation frequency in 10-Hz increments from 0 to 40 Hz. The force transducer was calibrated with metric weights. Results were analyzed by Pearson product-moment correlation to measure the strength of association between stimulation frequency and axial force. Values of P < 0.05 were considered significant.

RESULTS

Protocol 1: Effect of PC activation on pharyngeal Pbal. During quiet breathing under eucapnic conditions, the hyopharyngeus exhibited phasic expiratory activity, which progressively increased under hypercapnic conditions. Phasic hyopharyngeal activity at 9% end-tidal CO2 was 379 ± 215 (SD) % of its activity during eucapnia. During quiet breathing under eucapnic conditions, the cricothyroid was phasically active during inspiration in six cats and tonically active in the remaining two cats. Hypercapnia was associated with recruitment of respiratory-related cricothyroid activity in all cats. Under these conditions, cricothyroid discharge was predominantly biphasic, with peak activity occurring on inspiration in six cats and on expiration in the two cats with tonic activity during eupnea. In the six cats with phasic activity under normocapnic conditions, there was a 1,338 ± 1,257% increase in activity (median of 695%, and range between 480 and 4,000%) at 9% end-tidal CO2.

Figure 3 shows, in one cat, the close correlation between Pbal during expiration and the pattern of phasic PC discharge at different levels of end-tidal CO2. In the 10 cats, changes in phasic expiratory PC activity during progressive hyperoxic hypercapnia were directly related to changes in Pbal (Fig. 4). In contrast, the progressive decreases in Pbal during inspiration with progressive hypercapnia were not associated with significant changes in tonic PC activity. Severing of the superior laryngeal nerve was associated with a com-
plete loss of cricothyroid activity. After severing of the superior laryngeal nerve and tracheal immobilization, phasic PC activity decreased under hypercapnic conditions (Fig. 5). Despite this difference in activation, peak Pbal during expiration was significantly greater at severing of the superior laryngeal nerve and tracheal immobilization.

**Protocol 2: Effect of PC activation on pressure-volume relationships in the isolated, sealed pharyngeal airway.**

At resting volume, pressure in the isolated, sealed upper airway increased with increasing stimulation frequency up to a frequency of 40–50 Hz. Fusion of the contractile response occurred at 20 Hz. Stimulation above the fusion frequency was characterized by a bimodal pressure response, i.e., a relatively rapid increase to a maximum value, followed by a slower decrement to a plateau pressure. During stimulation in protocol 2, air was injected or withdrawn from the isolated, sealed airway only after a plateau pressure was reached. Unilateral stimulation of the nerve resulted in rotation of the ventral pharyngeal airway to the side of stimulation.

Figure 6 shows the typical pressure-volume relationships in the isolated, sealed pharyngeal airway in one cat with and without bilateral stimulation of the pharyngeal branch of the vagus nerve. The R² value for the third-order regression equations was 0.997 ± 0.002. For the group, airway compliance in the unstimulated or stimulated conditions progressively decreased with decreases in airway volume. Compared with the unstimulated condition, PC stimulation was associated with a decrease in compliance at resting volume and at a relatively low airway volume below resting volume (Table 1). In most animals, the decrease in compliance at a given volume from the unstimulated to the stimulated condition appeared to increase as airway volume decreased, but this change did not reach statistical significance (P = 0.69).

Airway pressures at given airway volumes with and without stimulation are shown in Table 1 and Fig. 7. At a relatively high airway volume above resting volume, PC stimulation increased airway pressure compared with that in the absence of stimulation. This constrictor effect was diminished at resting volume. At relatively low airway volumes below resting volume, the stimulated and unstimulated pressure-volume relationships crossed. The mean coordinates of the intersection point of the two curves were −6.72 ± 3.10 cmH₂O and −1.21 ± 0.38 ml. With further decrements in airway volume, airway pressure with PC stimulation decreased compared with that without stimulation.

**Protocol 3: Axial effects of pharyngeal constrictor activation.**

Bilateral stimulation of the pharyngeal branch of the vagus nerve resulted in an increase in rostrally directed axial force (Fig. 8). As described for the pressure signal in protocol 2, stimulation above the fusion frequency of 20 Hz was characterized by a bimodal response, a relatively rapid increase to a maximum value followed by a slower decrement to a plateau force. Both the maximum and plateau axial force were directly related to stimulation frequency over the frequency range of 0–40 Hz.

**DISCUSSION**

The results indicate that PC activation stiffens the pharyngeal airway. Airway compliance in the isolated, sealed upper airway preparation decreased with stimu-
ation of the motor output to the PC muscles at resting volume and airway volumes below resting volume. The results also indicate that PC activation has both radial and axial mechanical effects on pharyngeal airway function and that the radial effects are dependent on airway volume. In protocol 1, volume in the pharyngeal airway was fixed at a relatively high volume by the high-compliance balloon used to measure the pressure generated by the airway walls. In this protocol, an increase in respiratory-related PC activity was closely related to $P_{bal}$; this suggests that the PCs constrict the airway. The results of protocol 2 show that these radial effects are dependent on airway volume. In the isolated, sealed upper airway preparation used in protocol 2, bilateral electrical stimulation of the nerve carrying motor output to the PC muscles increased airway pressure at airway volumes at and above resting volume. As in protocol 1, the muscles functioned as constrictors. However, at relatively low airway volumes below resting volume, PC contraction decreased airway pressure. Under these conditions, the PCs were acting to dilate the airway. This functional duality is not unique to the PCs. De Troyer et al. (5) have shown that the external intercostal muscles can function as inspiratory or expiratory pump muscles of respiration depending on lung volume.

The results of protocol 1 must also be interpreted with caution. As reported previously in decerebrate cats, the results of protocol 1 demonstrate recruitment of phasic expiratory PC activation under hypercapnic conditions (16). The results also indicate a close association between phasic PC activity and pressure in the high-compliance balloon occluding the pharyngeal airway. As shown in Fig. 3, peak $P_{bal}$ in expiration lagged behind peak PC phasic activity. This phase lag may have been due in part to an electromechanical time constant. However, as shown in Fig. 5, rostral tracheal immobilization and cricothyroid muscle denervation resulted in greater increases in peak expiratory pressure under hypercapnic conditions; this suggests that the $P_{bal}$ results were influenced by factors other than PC activation. Van de Graaff (23) showed that upper airway resistance rostral to the glottis decreased with increased caudal tracheal movement, independent of upper airway muscle activation. Using computerized axial tomography, Amis et al. (1) demonstrated pharyngeal dilation associated with supramaximal electrical stimulation of the cricothyroid muscle in anesthetized dogs. Tonic activation of other pharyngeal muscles

![Fig. 5. Phasic PC EMG activity (A) and peak pharyngeal $P_{bal}$ (B) in all cats ($n=10$) during progressive hyperoxic hypercapnia before (Preclamp) and after (Clamped) immobilization of rostral tracheal cannula and severing of superior laryngeal nerve bilaterally. Each point represents mean ± SD of 5 breaths at a given level of $CO_2$ in 1 cat.](image)

![Fig. 6. Pressure-volume relationship in isolated, sealed upper airway without (○) and with (●) bilateral stimulation of pharyngeal branch of vagus nerve (25 Hz, 1-ms duration, 3 V). Lines, 3rd-order regressions through data. Stimulation at resting volumes at and above resting volume resulted in an increase in airway pressure (●). Stimulation at a relatively low airway volume resulted in a decrease in airway pressure (○). ΔVolume, change in volume.](image)

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<th>Table 1. Airway compliance and pressure measurements with and without pharyngeal constrictor stimulation</th>
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<td>Low Airway Volume</td>
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<td>Unstimulated compliance, ml/cmH$_2$O</td>
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<td>Stimulated compliance, ml/cmH$_2$O</td>
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<td>Change in compliance, ml/cmH$_2$O</td>
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Values are means ± SD. Low airway volume was 1.83 ± 0.35 ml below resting volume, and high airway volume was 0.90 ± 0.32 ml above resting volume. Change in compliance and pressure, change from stimulated to unstimulated condition.
under hypercapnic conditions may have influenced Pbal during expiration (24). Although tonic PC activity did not change with progressive hypercapnia, minimum pharyngeal Pbal on inspiration decreased, even after tracheal immobilization and cricothyroid denervation. This is probably attributable to the recruitment of pharyngeal airway muscles that dilate the airway by means of phasic inspiratory activity. Despite the probable influence of other upper airway muscles on Pbal in protocol 1, the close association between expiratory PC activation and peak expiratory Pbal is not surprising, given that the PC muscles are the only pharyngeal muscles known to exhibit phasic expiratory activation under hypercapnic conditions. Even the tongue retractor muscles, which also have a prominent role in swallowing, have recently been shown to exhibit phasic inspiratory activity during hypoxia and hypercapnia (6).

In protocols 2 and 3, the PC muscles were activated by electrically stimulating the nerves supplying their motor output. This nonphysiological stimulus was used to examine selectively the mechanical effects of PC activation in the absence of activation of other pharyngeal muscles. In protocol 2, the negative pressure generated by withdrawal of volume from the isolated, sealed upper airway may have recruited other upper airway muscles. However, measures were taken in this protocol to suppress activation of upper airway muscles by passively hyperventilating the animals and severing the superior laryngeal nerve, which carries most of the afferents from the laryngeal airway. Even if other upper airway muscles were reflexly activated by the negative intraluminal pressure in protocol 2, it is unlikely that this would have affected the results, because it would have occurred during both the control (unstimulated) and experimental (stimulated) conditions.

Figure 9 presents a schematic of the mechanical effects of PC activation on pharyngeal airway function. The PCs attach posteriorly on the relatively immobile pharyngeal aponeurosis and wrap around the airway to attach on moveable anterior pharyngeal structures, such as the hyoid bone and thyroid cartilage. In general, the posterior attachments of the muscle fibers are more rostral than the anterior attachments. Given this fiber orientation, the force generated by PC contraction has both a radial and axial component. The axial force is directed in a rostral direction. The direction of the radial force is dependent on airway volume. At relatively high airway volumes, the radial force is directed inward, promoting airway constriction. At relatively low airway volumes, the radial force is directed outward, promoting airway dilation.

The results of this study help to resolve some of the seeming paradoxes concerning PC muscle activation. The PCs promote airway closure during swallowing. But progressive hypercapnia and hypoxia elicit phasic expiratory PC activation in decerebrate cats and in normal adults during wakefulness. As shown in protocol 1, this respiratory-related activation will cause
pharyngeal constriction at high airway volumes. Clinically, however, hypercapnia and hypoxia are most likely to occur in human subjects with pathological narrowing or closure of the pharyngeal airway during sleep. The results of the current study suggest that respiratory-related PC activation under these conditions would help protect airway patency by stiffening and dilating the airway.

PC activation also generates an axial force on the pharyngeal airway. This rostrally directed axial force could help elevate laryngeal and pharyngeal structures, a prominent component of the pharyngeal phase of swallowing. It is likely that the axial force also plays a role in the respiratory-related function of the PC muscles. As postulated by Murakami and Kirchner (18), activation of PC muscles during expiration may help return pharyngeal structures to their resting position after their caudal displacement by tracheal tug during inspiration (23). Whereas lengthening of the upper airway during inspiration stiffens the airway (19), airway compliance would increase with airway shortening during expiration. As the airway shortens in expiration, phasic PC activation during expiration would help stiffen the airway, particularly at end expiration, when the airway is most susceptible to collapse (19, 20). PC activation at the termination of an apnea may be particularly effective in OSA subjects with low lung volumes caused by obesity and by exhalation of air during an obstructive apnea. At end apnea, the resulting decrease in tracheal tug would increase pharyngeal airway collapsibility. PC activation under these conditions would stiffen and dilate the airway, helping to maintain airway patency.

Our previous EMG study in normal, awake humans found PC activation during swallowing, respiration, and phonation (15). These EMG results support the general consensus that a given pharyngeal muscle participates in many different upper airway functions. The results of the current study concerning the mechanical effects of PC activation on pharyngeal airway function help explain how the PCs, and probably other pharyngeal muscles, play a role in these disparate functions. Based on the PC findings, the mechanical effects of a pharyngeal muscle may depend on the airway conditions under which it is activated. Rather than a separate set of muscles performing one particular function, the PC results predict that the pattern of activation of the pharyngeal airway muscles and the conditions under which they are activated allow a given muscle to have diagnostically different mechanical effects on the pharyngeal airway.

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