A threshold lung volume for optimal mechanical effects on upper airway airflow dynamics: studies in an anesthetized rabbit model

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Kairaitis K, Verma M, Amatoury J, Wheatley JR, White DP, Amis TC. A threshold lung volume for optimal mechanical effects on upper airway airflow dynamics: studies in an anesthetized rabbit model. J Appl Physiol 112: 1197–1205, 2012. First published January 12, 2012; doi:10.1152/japplphysiol.01286.2011.—Increasing lung volume improves upper airway airflow dynamics via passive mechanisms such as reducing upper airway extraluminal tissue pressures (ETP) and increasing longitudinal tension via tracheal displacement. We hypothesized a threshold lung volume for optimal mechanical effects on upper airway airflow dynamics. Seven supine, anesthetized, spontaneously breathing New Zealand White rabbits were studied. Extrathoracic pressure was altered, and lung volume change, airflow, pharyngeal pressure, ETP laterally (ETPlat) and anteriorly (ETPant), tracheal displacement, and sternohyoid muscle activity (EMG%max) monitored. Airflow dynamics were quantified via peak inspiratory airflow, flow limitation upper airway resistance, and conductance. Every 10-ml lung volume increase resulted in caudal tracheal displacement of 2.1 ± 0.4 mm (mean ± SE), decreased ETPlat by 0.7 ± 0.3 cmH2O, increased peak inspiratory airflow of 22.8 ± 2.6 cmH2O (all P < 0.02), and no significant change in ETPant or EMG%max. Flow limitation was present in most rabbits at baseline, and abolished 15.7 ± 10.5 ml above baseline. Every 10-ml lung volume decrease resulted in cranial tracheal displacement of 2.6 ± 0.4 mm, increased ETPant by 0.9 ± 0.2 cmH2O. ETPlat was unchanged, increased EMG%max of 11.1 ± 0.3%, and a reduction in peak inspiratory airflow of 10.8 ± 1.0% (all P < 0.01). Lung volume, resistance, and conductance relationships were described by exponential functions. In conclusion, increasing lung volume displaced the trachea caudally, reduced ETP, abolished flow limitation, but had little effect on resistance or conductance, whereas decreasing lung volume resulted in cranial tracheal displacement, increased ETP and increased resistance, and reduced conductance, and flow limitation persisted despite increased muscle activity. We conclude that there is a threshold for lung volume influences on upper airway airflow dynamics.

LUNG VOLUME has an important influence on the stability of the human upper airway. Studies, in both awake and sleeping subjects, confirm that increased end-expiratory lung volumes are associated with reduced pharyngeal collapsibility, increased pharyngeal size, and decreased pharyngeal airway resistance (2, 6, 10, 12). Current pathophysiological analyses of obstructive sleep apnea (OSA) recognize a role for interactions between lung volume and upper airway mechanics (19). For patients with pharyngeal anatomic compromise (3), nocturnal upper airway obstruction may occur as a result of both a sleep-related decrement in upper airway muscle activity (41) and a low resting lung volume, itself associated with horizontal posture, sleep, and obesity (28).

Investigations on the influence of lung volume change on upper airway have resulted in contrasting results in normal subjects and subjects with OSA. In healthy sleeping subjects, increasing lung volume has a small effect on pharyngeal collapsibility and resistance (27, 30), whereas in sleeping OSA subjects in response to increasing lung volume there is a marked reduction in upper airway collapsibility (12), severity of sleep-disordered breathing (9), and the level of continuous positive airway pressure (CPAP) required to abolish flow limitation (8). When lung volume is decreased during sleep in healthy subjects upper airway resistance increases and pharyngeal collapsibility increases (27, 30); however, in OSA subjects there is little further decline in pharyngeal collapsibility (29), and only a slight increase in CPAP requirements to abolish flow limitation (8). The different responses between healthy and OSA subjects may be due to differences in the resting lung volume during sleep.

There may also be differences in the underlying mechanics determining upper airway patency. Animal models have demonstrated inspiratory-related tracheal displacement transmits traction forces to the pharyngeal airway wall, resulting in enhanced upper airway patency (24, 31–35). Increased lung volume itself is hypothesized to enhance upper airway function through tracheal displacement, resulting in a combination of increased longitudinal wall strain and reduced surrounding tissue pressure (23, 24, 31). We have since confirmed, in an animal model, that caudal tracheal displacement does reduce peri-pharyngeal extraluminal tissue pressure (ETP) levels (13). More recently, in an enclosed chamber Starling resistor bench model, a mechanical model of the upper airway, we demonstrated a unique longitudinal wall strain level (equated to tracheal displacement) associated with decreased collapsibility and optimal airflow dynamics in the face of increasing surrounding positive chamber pressure (equated to ETP) (1). This observation of an optimal longitudinal strain in a bench model led us to speculate that a similar condition may exist in vivo and may explain different responses between healthy and OSA subjects based on individual relationships between operating and optimal lung volumes.

We hypothesize that there is a threshold lung volume for preventing both increased upper airway airflow resistance and the development of inspiratory airflow limitation. The aim of
the present study was to utilize an anesthetized rabbit model to explore interactive effects between lung volume, tracheal displacement, peri-pharyngeal tissue pressure, peak inspiratory airflow, and upper airway airflow resistance and conductance.

**METHODS**

**Subjects.** Studies were performed on seven adult, male, supine, spontaneously breathing New Zealand White rabbits. The protocol was approved by the Sydney West Area Health Service Animal Ethics Committee.

**Anesthesia.** Anesthesia was maintained via a continuous intravenous infusion (ear vein) of ketamine (15 mg·kg⁻¹·h⁻¹) and xylazine (4.5 mg·kg⁻¹·h⁻¹).

**Experimental set-up.** Animals were positioned head out in a sealed perspex box with ports to allow measurement and manipulation of box pressure and with head/neck position controlled such that a line drawn from the tragus to the external nares was at 50° to the horizontal (Fig. 1). A loose seal, which could be closed to reduce leak but which did not compress the neck, was created around the neck using a sleeve (Fig. 1). A loose seal, which could be closed to reduce leak but which did not compress the neck, was created around the neck using a sleeve (4.5 mg·kg⁻¹·h⁻¹).

**Measurement of upper airway extraluminal tissue pressure.** The ETP was measured using pressure transducer-tipped catheters (MPC 500, Millar Instruments, Houston, TX) surgically inserted into the tissues surrounding the pharyngeal airway as previously described (15). Briefly, pressure was measured in the pharyngeal submucosal tissues at the level of the angle of the mandible for 1) the right lateral pharyngeal wall ETP (ETPplat); and 2) the anterior pharyngeal wall ETP (ETPant) below the tongue, midline in the coronal plane. Correct positioning of each catheter was verified via postmortem dissection at the conclusion of each study.

**Measurement of tracheal displacement.** A midline incision was made over the anterior surface of the neck and the trachea was exposed. The 3rd cranial tracheal ring was marked, and its end-expiratory position (tracheal displacement, TD) tracked manually from a newborn humidifier.

**Measurement of airflow and pressures.** Respiratory airflow (V) was measured using a heated pneumotachograph (Hans-Rudolph 8300A, Hans Rudolph, Kansas City, MO) attached to a tightly sealed face-mask. Pharyngeal lumen pressure (Pph) was measured using a pressure transducer-tipped catheter (SPR 524, Millar Instruments, Houston, TX) inserted retrogradely through a 20-gauge cannula inserted into the trachea through the larynx into the pharynx to just above the epiglottis. The cannula was removed after insertion of the catheter and correct positioning was confirmed at postmortem.

**Measurement of upper airway muscle activity.** Using a 23-gauge needle, bipolar, teflon-coated stainless steel wire electrodes (0.003-in. bare, 0.0055-in. coated, SDR Technology, Sydney, Australia) were inserted into the belly of the right sternohyoid muscle, a representative upper airway dilator muscle in rabbits (17, 22). Correct placement of electrodes was assessed by identifying characteristic movements in response to application of an electrical stimulus to the implanted wires, as described by Van der Touw and colleagues (36), and by identification of an increase in inspiratory activity during nasal obstruction. The raw signal was filtered (100–1,000 Hz), amplified, rectified, and passed through a leaky integrator (Neotrace NT 1900) with a time constant of 200 ms to produce a moving time average signal.

**Experimental protocol.** Starting from spontaneous resting EELV in the supine posture, graded negative and positive extrathoracic pressures (PET: −20 to +10 cmH₂O, in 2- to 5-cmH₂O increments) were applied to the external surface of the rabbit body via a positive/negative pressure source connected to the perspex box. Each run of graded pressure application was repeated three times.

**Data analysis.** The airflow signal from the sealed face mask was integrated to obtain volume, and the change in end-expiratory lung volume (ΔEELV) with each PET application measured from the calibrated volume channel by measuring the difference between the volume signal at end expiration immediately prior to change in PET and on the third to fifth breath after the change. Peak inspiratory airflow was averaged over five breaths for each ΔEELV, and airflow limitation determined from inspection of the pressure-airflow relationship. Peak inspiratory airflow was expressed as percent of baseline airflow. Change in baseline average ETP (ΔETP) values were measured for each level of PET.

To measure upper airway resistance (RUA), power functions (Pph = aVᵇ + c, where a, b, and c are constants) were fitted to the inspiratory limb of pressure-airflow curves from V = 0 to 20 ml/s, generated from five steady-state breaths at each PET level, and upper airway resistance (RUA = Pph/V at inspiratory V = 20 ml/s) was then calculated and expressed as a percentage of baseline RUA [RUA (%baseline)]. Upper airway conductance (GUA) was also calculated (1/RUA) and expressed as a percentage of baseline [GUA.
RESULTS

Application of graded subatmospheric Pet resulted in progressive increases in EELV in all rabbits while positive Pet were associated with reduced EELV. Typical raw data traces from one rabbit are shown in Fig. 2.

EELV and tracheal displacement. For the group, the most negative Pet applied (−15.5 ± 3.4 cm H2O) resulted in a 32.9 ± 10.4 ml increase in EELV and caudal tracheal displacement of 6.7 ± 1.9 mm, while maximum applied positive Pet (11.7 ± 3.3 cmH2O) resulted in a decrease in EELV of 14.5 ± 6.6 ml accompanied by cranial tracheal displacement of −4.0 ± 1.2 mm. Using linear mixed effects modeling, increasing EELV was associated with increasing cranial tracheal displacement at a rate of 0.21 ± 0.04 mm/ml ∆EELV (P < 0.0001; Fig. 3, A and C) while decreasing EELV related cranial tracheal displacement was −0.26 ± 0.04 mm/ml ∆EELV (P < 0.0001; Fig. 3, A and C).

Peak inspiratory sternohyoid activity. Increasing EELV resulted in no consistent change in peak inspiratory sternohyoid EMG activity (Figs. 2A and 3, B and D; P > 0.7, linear mixed effects model) whereas for every 10-ml reduction in EELV peak inspiratory sternohyoid EMG activity increased by 11.1 ± 0.3% (P < 0.0003; Figs. 2B and 3, B and D), due to increases in both phasic and tonic components (see Fig. 2B).

Upper airway extraluminal tissue pressures (ETP). Increasing EELV was associated with decreased peri-pharyngeal tissue pressure, particularly ETPant, while decreased EELV was associated with increased peri-pharyngeal tissue pressure, particularly ETPan. For the group, increasing EELV was associated with a fall in ETPant from a baseline of 5.4 ± 0.3 cmH2O to 2.3 ± 0.5 cmH2O at maximal ∆EELV. For every 10-ml increase in EELV, ETPant fell by 0.7 ± 0.3 cmH2O (Fig. 4, A and C; P < 0.02, linear mixed effects model). ETPan also fell with increasing EELV in all but one rabbit (Fig. 4B) and for the group from 3.5 ± 0.4 cmH2O at baseline to 2.0 ± 4.3 cmH2O at maximal ∆EELV. However, linear mixed effects modeling failed to identify a significant relationship between ETPan and ∆EELV for the group (Fig. 4, B and D; P = 0.2).

For the group, decreasing EELV resulted in an increase in 7.0 ± 3.9 cmH2O at maximal ∆EELV for ETPan and to 4.9 ± 3.5 cmH2O for ETPant. Although ETPant increased with decreasing EELV in all rabbits (Fig. 4A) this relationship did not achieve significance (Fig. 4C, P = 0.09) whereas ETPan increased significantly by 0.9 ± 0.2 cmH2O for each 10-ml fall in EELV (Fig. 4, B and D; P < 0.0001).

Upper airway resistance. Increasing EELV resulted in only a small reduction in RUA(%baseline) (Fig. 5A), whereas decreased EELV was associated with substantial increases in RUA(%baseline) for most rabbits. The relationship between RUA(%baseline) and ∆EELV for all levels of muscle recruitment was described by an exponential function RUA (%baseline) = 33.2 + 70.1·exp(−0.05·∆EELV) (R² = 0.48). For data
obtained under “low recruitment” conditions the overall relationship between RUA(%baseline) and EELV was described by the exponential function $RUA(%baseline) = 45.8 + 59.8 \times e^{-0.08 \times \text{EELV}}$ ($R^2 = 0.71$, Fig. 5B). Under “high recruitment” conditions RUA values were more variable with only some rabbits able to partially reduce the steep rise in RUA associated with reduced EELV. For the “high recruitment” group the relationship between RUA and EELV was described by the exponential function $RUA = 30.3 + 71.3 \times e^{-0.04 \times \text{EELV}}$ ($R^2 = 0.45$; Fig. 5C).

**Upper airway conductance.** When expressed as conductance, the relationship between EELV and GUA(%baseline) at all levels of muscle recruitment was described by the exponential function $GUA\% = 928.8 - 910.4 \times e^{-(\Delta\text{EELV} + 32.41)/290.9}$. For data obtained under “low recruitment” conditions the relationship was described by the function $GUA\% = 199.26 - 191.4 \times e^{-(\Delta\text{EELV} + 24.9)/30}$. For data obtained under “high recruitment” conditions the relationship was $GUA\% = 15,591 - 15,578 \times e^{-(\Delta\text{EELV} + 32.41)/4,867.4}$.

**Flow limitation and peak inspiratory airflow.** At starting EELV, inspiratory airflow limitation was detected in all but one of the rabbits (Fig. 6). When expressed as conductance, the relationship between ΔEELV and GUA(%baseline) at all levels of muscle recruitment was described by the exponential function $GUA\% = 928.8 - 910.4 \times e^{-(\Delta\text{EELV} + 32.41)/290.9}$. For data obtained under “low recruitment” conditions the relationship was described by the function $GUA\% = 199.26 - 191.4 \times e^{-(\Delta\text{EELV} + 24.9)/30}$. For data obtained under “high recruitment” conditions the relationship was $GUA\% = 15,591 - 15,578 \times e^{-(\Delta\text{EELV} + 32.41)/4,867.4}$.

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**Flow limitation and peak inspiratory airflow.** At starting EELV, inspiratory airflow limitation was detected in all but one of the rabbits (Fig. 6). For the group, increasing EELV above a threshold of 15.7 ± 10.5 ml (range 0–28.6 ml) completely eliminated airflow limitation and increased peak inspiratory flow levels whereas decreasing EELV airflow limitation persisted (Figs. 6 and 7). There was a significant positive linear relationship between increasing EELV (for non-airflow-limited breaths) and peak inspiratory airflow values (%baseline) (Fig. 7; $R^2 = 0.39$, $P < 0.0001$). During airflow limitation there was also a positive linear relationship between increasing EELV and peak inspiratory airflow (%baseline) (Fig. 7; $R^2 = 0.39$, $P < 0.0001$). Muscle recruitment had no effect on the slopes of the lines (all $P > 0.05$ for comparison of slopes of lines obtained under all recruitment conditions).

**DISCUSSION**

This is the first study to describe relationships between end-expiratory lung volume, tracheal displacement, upper airway airflow dynamics, and upper airway extraluminal tissue pressure and to define a threshold lung volume for the onset of flow limitation. The relationships between upper airway resistance, upper airway conductance, and lung volume as demonstrated for the upper airway in the present study are analogous to those first described for the lower respiratory tract more than six decades ago (4), suggesting a commonality of mechanistic linkage mediated via effects on airway wall stiffness and surrounding expansion or compression forces.
Critique of methods. Lung volume was altered via application of pressure to the surface of the rabbit body below the neck, which may have other physiological effects. In particular, it may redistribute blood volume cranially, and this may have had a direct effect on upper airway patency through alterations in central venous pressures. Alternatively, the development of pressure gradients from the thorax to the neck may have contributed to the alterations in surrounding peri-pharyngeal tissue pressures.

Measurement of ETP is an invasive process, the limitations of which have been discussed previously. Most notably, the presence of a catheter tip in the peri-pharyngeal tissues likely results in an alteration in the absolute value of the pressure measured. Accordingly, we have focused on change in ETP rather than absolute value.

Lung volume was measured as a change from baseline using the integrated flow signal from a pneumotachograph. Thus we have not measured absolute EELV, but rather change from spontaneous resting levels, defined as the lung volume when Per was atmospheric. The animals in this study were supine and anesthetized, both of which are likely to reduce resting lung volume. Consequently, lung volume in this study is likely to be less than functional residual capacity (FRC) in an awake, upright animal. However, reduced lung volume associated with supine posture and anesthesia in our model would mimic that experienced by supine, sleeping humans.

The trachea was exposed surgically to allow for measurement of tracheal displacement. This may have resulted in some disruption to the interactions between the upper airway and lower airway; however, every effort was made to minimize the extent of the surgical intervention.

The sternohyoid muscle was chosen as a representative upper airway dilator muscle as it has been shown in rabbits to have similar inspiratory phasic activity as the genioglossus muscle, and similar falls in upper airway resistance when stimulated to contract.

The upper airway resistance measurement was performed at a relatively low inspiratory airflow level (common to all rabbits and conditions; 20 ml/s) as this measurement can only be performed over a non-flow-limited part of the pressure/flow relationship. Peak inspiratory flow values, however, are measured either at flow limitation or higher up the pressure/flow relationship. Upper airway collapsibility was not measured directly, but inferred from presence or absence of airflow limitation. The onset of airflow limitation in a Starling resistor model indicates the onset of dynamic tube wall collapse and represents the point at which the driving pressure for airflow is now the transmural pressure, rather than the difference between upstream and downstream pressure. Thus the onset of inspiratory airflow limitation in the present study can be considered to be the point at which upper airway wall collapses during inspiration.
Threshold lung volume for upper airway collapse: evidence from peak inspiratory airflow and airflow limitation. The presence of airflow limitation is an indication that the upper airway is collapsible. Loss of airflow limitation occurred at ~16 ml above resting end-expiratory lung volume, suggesting that an increase in lung volume equivalent to approximately one tidal volume (~20 ml in a rabbit) results in sufficient stiffening to prevent airway collapse. Thus for airflow collapsibility and associated airflow limitation there appears to be a threshold operating point, within one tidal volume above the spontaneous resting end-expiratory lung volume in a supine anesthetized rabbit, whereby a reduction in end-expiratory lung volume results in persistent airflow limitation accompanied by modest falls in peak inspiratory airflow, while an increase in end-expiratory lung volume leads to loss of airflow limitation and continuing increases in peak inspiratory airflow. Upper airway dilator muscle recruitment did not alter the increased collapsibility associated with end-expiratory lung volume below this threshold as there was equivalent airflow limitation and reduced peak inspiratory airflow in both the “low” and “high” muscle recruitment groups.

Threshold lung volume for upper airway patency: evidence from RUA and GUA. The lumen radius is critical in determining resistance (37), whereas airway length has only a small influence. Thus it seems that at the threshold end expiratory lung volume, upper airway size itself is at a threshold point below which any further decrease in lumen size dramatically increases upper airway resistance while modestly reducing upper airway conductance, whereas increasing lumen size above this threshold has minimal impact on an already low resistance but causes conductance to increase. Upper airway muscle activity modified these relationships in a variable manner between rabbits, but overall was unable to counteract the increase in upper airway resistance or fall in conductance associated with decreasing end-expiratory lung volume.

Tracheal displacement. Caudal tracheal displacement and mediastinal traction are thought to be the primary source for lung volume-related changes in longitudinal upper airway wall strain (35). In the present study tracheal displacement was linearly related to change in end-expiratory lung volume. Increasing lung volume resulted in maximum caudal tracheal displacement values of ~7 mm, a similar value to that associated with application of 48 g force directly to the caudal end of the transected rabbit trachea in our previous study (13). On the other hand, decreasing EELV was associated with a maximum cranial tracheal displacement of ~4 mm.

In our previous study we concluded that tracheal traction stabilized the upper airway by both a reduction in ETP, and increasing longitudinal strain (14). Increasing tracheal displacement increases upper airway wall strain; however, the amount will vary due to structural heterogeneity of the trachea and pharyngeal airway. Reductions in ETP in the tissues have likely occurred in response to tissue movement. Mechanically this is a reduction in stress in the tissues, which will have two components: volumetric, likely proportional to the ETP measurement, and shear stress which may not have been measured. Given previous analyses of the effect of tracheal traction on upper airway mechanics (13, 23, 24), including our recent bench study (1), it is likely that reduced upper airway wall longitudinal strain contributed to deterioration in upper airway function at low lung volumes. On the other hand increasing upper airway wall strain with increasing lung volumes may have contributed to decreased collapsibility and increasing upper airway size.
**Peri-pharyngeal tissue pressure.** We have previously reported that increased caudal tracheal traction in anesthetized rabbits lowers ETP in peri-pharyngeal tissue regions similar to those monitored in the present study (13). However, the ETP reduction reported earlier of 0.2–0.5 cmH₂O at 6-mm tracheal displacement were much less than the maximum change of 1.5–2 cmH₂O at maximal EELV around 7-mm tracheal displacement measured in the present study. This is likely because reductions in ETP result not just from tracheal displacement but also from caudal movement of other structures in the neck. In earlier studies, Van de Graaf (35) demonstrated that to abolish lung volume related improvement in upper airway patency, all the mediastinal connections between the upper and lower airway needed to be severed.

Increased peri-pharyngeal tissue pressure increases upper airway transmural pressure, thus tending to narrow the upper airway and contributing to an increase in \( R_{UA} \) (14), whereas decreased peri-pharyngeal tissue pressure reduces this effect (16). In the passive airway, interactions with wall strain likely determine the resultant impact on upper airway patency and collapsibility (1, 13, 23, 24). In the present study this interaction produced optimal flow dynamic upper airway geometry just above supine anesthetized spontaneous resting EELV.

**Sternohyoid muscle recruitment.** Negative upper airway luminal pressure is well known to recruit upper airway dilator muscle activity (38, 39) and in this case upper airway intraluminal pressures fell in association with increasing upper airway resistance as end-expiratory lung volume was reduced.

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*Fig. 6. Data from individual rabbits (A–G) showing the % of breaths flow limited with each change in end-expiratory lung volume (ΔEELV). Each symbol represents the result for each of the 3 runs, and the shaded area represents the overlap for flow limitation for each of the 3 runs. Note that in every rabbit there is a threshold lung volume for the onset of flow limitation, where the flow limitation is completely abolished. Note also that between rabbits there is a range for this threshold (0–28 ml); however, in all rabbits loss of flow limitation occurs within one tidal volume (~20 ml in a rabbit) of resting lung volume.*
Other mechanisms such as autonomic and chemoreceptor activity may also have been modulating muscle activity (11). The impact on upper airway collapsibility and geometry associated with low lung volume, however, appears to have been of such magnitude that upper airway dilator muscle recruitment was insufficient in most rabbits to prevent increased upper airway resistance and the development of inspiratory airflow limitation.

Threshold lung volume for upper airway airflow dynamics. This study leads us to speculate that the interaction between upper airway airflow limitation, resistance, and conductance and lung volume is regulated around a threshold lung volume (see Fig. 8) in a similar manner to that demonstrated for longitudinal strain and tube function in our earlier bench study of a Starling resistor (1). These findings suggest 1) compromised anatomy and increased collapsibility at lung volume below the threshold lung volume; 2) “optimized” anatomy (for flows of 20 ml/s) at (and above) the threshold lung volume; and 3) reduced upper airway collapsibility and increased upper airway size at higher lung volumes. These mechanical outcomes are associated at low lung volumes with increased peri-pharyngeal tissue pressures combined with reduced upper airway longitudinal strain and at high EELV with decreased peri-pharyngeal tissue pressures combined with increased upper airway longitudinal strain (see Fig. 8).

Implications for OSA and maintenance of upper airway patency. The outcome of interventions aimed at decreasing sleep disordered breathing in OSA patients via alterations in lung volume will depend on the relationship between the actual lung volume and the threshold lung volume, as modified by the level and effectiveness of upper airway dilator muscle recruitment (see Fig. 8). Consequently, interpretation of studies examining interactions between lung volume and upper airway function in sleeping OSA patients may require an understanding of individual subject relationships between existing and threshold lung volume.

Conclusion. We conclude that there is a threshold for lung volume influences on upper airway airflow dynamics. If lung volume falls below this threshold level, upper airway resis-

tance increases substantially, flow limitation develops, and upper airway conductance falls, as a result of increased peri-pharyngeal tissue pressure and decreased upper airway wall longitudinal strain. The magnitude of this deterioration in upper airway airflow dynamics is modified variably between subjects by concomitant upper airway dilator muscle recruitment. On the other hand increasing lung volume above threshold levels results in little change in upper airway resistance but reduces collapsibility and increases upper airway conductance, with little associated increase in upper airway dilator muscle activity. These findings have implications for understanding the role of lung volume in the pathogenesis and treatment of obstructive sleep apnea.

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Fig. 7. Data demonstrating the relationship between change in end-expiratory lung volume (ΔEELV) and peak inspiratory airflow (% baseline) for non-flow-limited breaths (open circles) and flow-limited breaths (closed circles). Note that increasing end-expiratory lung volume increased peak airflow, while reductions in end-expiratory lung volume resulted in a lesser fall in peak inspiratory airflow across already flow-limited breaths. Gray lines represent regression lines for non-flow-limited breaths ($R^2 = 0.57$, $P < 0.0001$) and flow-limited breaths ($R^2 = 0.39$, $P < 0.0001$).

Fig. 8. Relationships between upper airflow limitations and change in end-expiratory lung volume (ΔEELV) in a supine anesthetized rabbit model. Plotted lines represent fitted exponential functions obtained from the data under “low recruitment” conditions for upper airway resistance ($RUA$, expressed as % baseline) (gray line) and upper airway conductance ($GUA$, expressed as % baseline), or linear regression fits (dashed gray lines) for peak inspiratory flow during flow limitation (left-hand line) or no flow limitation (right-hand line). Vertical dashed line represents the resting volume of the lung ($ΔEELV = 0$), and the solid vertical line represents the average position (threshold volume) for all animals at which flow limitation was lost ($ΔEELV = 15.7$ ml). Shading represents the zone where flow limitation is present. Note that for increases in end-expiratory lung volume above the threshold lung volume of 15.7 ml, there is a small fall in $RUA$ (%baseline), a slight increase in $GUA$ (%baseline), a loss of flow limitation, with a fall in ETP, and an increase in tracheal displacement. In contrast, lowering of the EELV below this threshold results in the onset of flow limitation, a marked increase in $RUA$ (%baseline), a reduction in $GUA$ (%baseline), associated with an increase in ETP and a fall in tracheal displacement.
DISCLOSURES

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

AUTHOR CONTRIBUTIONS


REFERENCES


