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Mediastinal Masses, Anesthetic Interventions, and Airway Compression in Adults: A Prospective Observational Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- There is a serious concern that muscle paralysis and positive pressure ventilation of a patient with a large mediastinal mass may worsen the compressed airway segment and lead to an inability to ventilate
- Classic teaching is that maintaining spontaneous breathing is safer and preserves airway patency compared to positive pressure ventilation and/or paralysis
- However, there is a lack of evidence to support such a notion

What This Article Tells Us That Is New

- This prospective, single-center, observational study measured the dynamic change in the anterior–posterior diameter of the segment of the compressed central airway during staged induction of 17 adult patients with large mediastinal masses
- The compression of the central airway in a semisitting position did not worsen after muscle paralysis or muscle paralysis plus positive pressure ventilation compared with that occurring during awake, spontaneous breathing

ABSTRACT

Background: Central airway occlusion is a feared complication of general anesthesia in patients with mediastinal masses. Maintenance of spontaneous ventilation and avoiding neuromuscular blockade are recommended to reduce this risk. Physiologic arguments supporting these recommendations are controversial and direct evidence is lacking. The authors hypothesized that, in adult patients with moderate to severe mediastinal mass–mediated tracheobronchial compression, anesthetic interventions including positive pressure ventilation and neuromuscular blockade could be instituted without compromising central airway patency.

Methods: Seventeen adult patients with large mediastinal masses requiring general anesthesia underwent awake intubation followed by continuous video bronchoscopy recordings of the compromised portion of the airway during staged induction. Assessments of changes in anterior–posterior airway diameter relative to baseline (awake, spontaneous ventilation) were performed using the following patency scores: unchanged = 0; 25 to 50% larger = +1; more than 50% larger = +2; 25 to 50% smaller = –1; more than 50% smaller = –2. Assessments were made by seven experienced bronchoscopists in side-by-side blinded and scrambled comparisons between (1) baseline awake, spontaneous breathing; (2) anesthetized with spontaneous ventilation; (3) anesthetized with positive pressure ventilation; and (4) anesthetized with positive pressure ventilation and neuromuscular blockade. Tidal volumes, respiratory rate, and inspiratory/expiratory ratio were similar between phases.

Results: No significant change from baseline was observed in the mean airway patency scores after the induction of general anesthesia (0 [95% CI, 0 to 0]; $P = 0.953$). The mean airway patency score increased with the addition of positive pressure ventilation (0 [95% CI, 0 to 1]; $P = 0.024$) and neuromuscular blockade (1 [95% CI, 0 to 1]; $P < 0.001$). No patient suffered airway collapse or difficult ventilation during any anesthetic phase.

Conclusions: These observations suggest a need to reassess prevailing assumptions regarding positive pressure ventilation and/or paralysis and mediastinal mass–mediated airway collapse, but do not prove that conventional (nonstaged) inductions are safe for such patients.

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Life-threatening central airway collapse and/or cardiovascular collapse are well-known risks associated with general anesthesia in patients with large mediastinal masses.[1–3] The mechanisms of cardiovascular instability in this setting have been experimentally identified[4] while those of central airway obstruction remain ill-defined and largely uninvestigated.

When general anesthesia is unavoidable, recommendations to prevent airway collapse have been dictated by the enduring belief that maintenance of spontaneous ventilation and avoidance of neuromuscular blockade are superior to positive pressure ventilation and paralysis for the preservation of patency of extrinsically compressed central airways.[1,3,5–8] This decades-old foundational

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premise has, to our knowledge, never been experimentally verified.

A recent single-pilot observation by three authors from this group[9] failed to support those assumptions. We hypothesized that, in adult patients with moderate to severe mediastinal mass–mediated tracheobronchial compression, anesthetic interventions including positive pressure ventilation and neuromuscular blockade could be instituted without clinically significant compromise of central airways. We conducted a prospective observational study to evaluate the step-wise effects of general anesthesia, positive pressure ventilation, and neuromuscular blockade on airway patency using real-time video of bronchoscopic recordings taken during staged inductions on patients with moderate to severe tracheobronchial compromise.

Materials and Methods

This study was approved by the Institutional Review Boards of both institutions (Brigham and Women's Hospital; University of Virginia Health System). Patients with radiographically large mediastinal masses and/or evidence of moderate to severe airway compression observed *via* chest computed tomography and who were scheduled for procedures with general anesthesia were recruited between 2016 and 2020, after written informed consent was obtained. Exclusion criteria included: pregnancy; less than 18 yr old; prisoner status; and refusal by patient, surgeon, or anesthesiologist assigned to the case. A data analysis and statistical plan was written after the data was accessed.

After venous and radial arterial catheter insertion and mild sedation, patients were positioned in the operating room with their backs raised to comfort. All patients expressed a preference for 30- to 45-degree elevation of the head of the bed for ease of breathing. Airways were topically anesthetized with aerosolized 2% lidocaine and sedation was titrated, if desired, to maintain a verbally interactive state. Awake fiberoptic placement of an 8.5-mm (inner diameter) endotracheal tube or supraglottic airway device was performed, followed by application of supplementary topical lidocaine to the glottis or distal airway as needed. The video bronchoscope (EVIS EXERA III BF-1TH190; Olympus Medical Systems Corp., Japan) with high-definition resolution and 6.0-mm external diameter was then positioned with a view of the most stenotic region of the trachea or mainstem bronchus.

Continuous video recording was then performed through each phase of a staged induction: (1) awake with spontaneous ventilation; (2) anesthetized with spontaneous ventilation; (3) anesthetized with positive pressure ventilation; and (4) anesthetized with positive pressure ventilation and neuromuscular blockade. The airway device was connected to the anesthesia circuit by a swivel bronchoscope adaptor with 2 to 6 l/min oxygen (inspiratory oxygen fraction = 1.0) flows without added positive end-expiratory pressure (PEEP). Induction was performed by sevoflurane inhalation and confirmed by processed electroencephalogram (bispectral index [BIS Medtronic-Covidien, Ireland] less than 60), loss of lid reflex, and loss of response to verbal or physical stimulus. Positive pressure ventilation was applied thereafter *via* manual bag ventilation by a dedicated assistant instructed to match the same pattern (tidal volume [V_T]), inspiratory/expiratory ratio, respiratory rate [RR], and flow- *vs.* time-pattern) as that occurring during general anesthesia with spontaneous ventilation. Neuromuscular blockade was induced with either succinylcholine or a nondepolarizing agent and confirmed by twitch monitor, followed by a recording period as previously discussed.

To ensure safety, protocol dictated that in the event of airway closure, near-closure, inadequate ventilation, or hemodynamic instability, the recording protocol would terminate, and appropriate rescue maneuvers would be initiated. An *a priori* plan devised to treat worsening tracheal collapse was developed and included (1) bronchoscopically-guided intubation distal to the obstruction to stent the airway; and (2) availability of a rigid bronchoscope or extracorporeal support at the discretion of the anesthesiologist or surgeon.

Raw videos were reviewed by at least two experienced bronchoscopists, and clips were extracted representing each phase of the staged induction for each patient. The video segments for each phase were chosen with attention to selection of segments that were at least 20 s in duration and provided the clearest view of the most compressed portion of the airway, with minimal secretions, suctioning, or blurriness.

Scoring of the airway caliber as assessed by anterior–posterior diameter, relative to baseline (awake, spontaneous ventilation) was made separately by seven experienced bronchoscopists. Judges viewed clips one at a time in random, in scrambled order for each patient, blinded to which patient or phase of the staged induction they were viewing, and with the baseline clip displayed as a continuous loop for side-by-side comparison on identical size computer screens. Scoring was based on gross assessments across multiple respiratory cycles of anterior–posterior diameter changes in the region of maximal compression, disregarding background motion from inspiration/expiration, heartbeats, and bronchoscope movement. Such background motion could not be eliminated, and since it was not possible to mark which specific video frames corresponded to which portion of the respiratory cycle, fine distinctions based on respiratory cycle could not be evaluated. Judges were provided with a drawing depicting 0%, 25%, and 50% changes in anterior–posterior diameter for reference.

Statistical Analysis

For analytic purposes, airway anterior–posterior dimension changes were converted to central airway patency scores as follows: unchanged = 0; 25 to 50% larger = +1; more

than 50% larger = +2; 25 to 50% smaller = −1; more than 50% smaller = −2. Central airway patency scores (−2 to +2), derived from scoring of airway anterior–posterior diameters are presented as means with 95% CIs at each stage of anesthetic intervention. Anterior–posterior diameter changes greater than 50% were considered to be clinically significant. Comparison of central airway patency scores was performed using a linear mixed model which included intercepts for each subject/anesthetic intervention stage combination and separate random intercepts for each rater. Interrater reliability was estimated using the interclass correlation coefficient. Anesthetic stage was included as a fixed effect. Interrater reliability was estimated using the interclass correlation coefficient. Interrater reliability was estimated using the interclass correlation coefficient. No statistical power calculation was conducted; the sample size was based on the available data. All hypothesis testing was two-tailed (R version 4.1.0; R Foundation for Statistical Computing, Austria) and the statistical criterion for significance was $P < 0.05$.

Results

Twenty-one patients were recruited and studied between 2016 and 2020. Results from four were lost due to inadequate or irretrievable video bronchoscopy data. No patients were excluded or had their studies interrupted due to airway collapse, difficulties with ventilation, or hemodynamic instability. Video bronchoscopy images for two patients (no. 8 and no. 15) were incomplete (a total of three time points were missing), but the stages with satisfactory video data were included in the aggregate data analysis. It should be noted that similar images and observations from patient no. 1 were previously reported.[9] Patient and mass characteristics of the 17 subjects are shown in tables 1 and 2. The presence or absence of orthopnea was not reliably recorded in patients' records, and therefore was omitted from table 1. However, six patients had documented severe orthopnea (no. 1, no. 5, no. 6, no. 14, no. 16, and no. 17), and all patients were positioned to stated breathing preference in a semisitting position for this study. Computed tomographic scan–based cross-sectional areas of the central airways at the most compressed region were determined by the method of Cotton–Myer[10,11] as follows: less than or equal to 50% = I; 51 to 70% = II; more than 70% = III; and complete occlusion = IV.

Mean (95% CI) airway patency scores for the different phases of a staged induction are shown in figure 1A. Compared to baseline, the transition to general anesthesia was neither associated with a statistically significant (0 [95% CI, 0 to 0]; $P = 0.953$) change in the mean airway patency score nor a clinically significant decrease (mean estimate greater than 50%) in anterior–posterior diameter in any single patient. The mean airway patency score increased significantly and sequentially—first with the initiation of positive pressure ventilation (0 [95% CI, 0 to 1]; $P = 0.024$) and then, as increase persisted, with neuromuscular blockade (1 [95% CI, 0 to 1]; $P < 0.001$)—relative to that of the awake, spontaneous ventilation state. Distribution of anterior–posterior airway evaluations by phase are presented in figure 1B. Airway patency scores for different phases of a staged induction for individual subjects are shown in figure 2. The type-2 intraclass correlation coefficient, which was used to assess agreement among raters, was estimated to be 0.52 (95% CI, 0.42 to 0.64). Although this intraclass correlation coefficient value is generally indicative of moderate reliability, it may be influenced by the discrete nature of the data, and the intraclass correlation coefficient may to some extent obscure the reliability of the agreement. For example, across all combinations of patients and anesthetic phases, 70% of ratings match the median rating for the patient and phase, only 1% of ratings differed from the median by two categories, and no ratings were more than two categories from the median.

Representative still images for two subjects (no. 3 and no. 10) are presented in figures 3 and 4, respectively. Computed tomographic images, virtual bronchoscopic images, and still bronchoscopic images for all 17 subjects are provided in Supplemental Digital Content (1 [http://links.lww.com/ALN/C701], 2 [http://links.lww.com/ALN/C702], 3 [http://links.lww.com/ALN/C703], 4 [http://links.lww.com/ALN/C704], 5 [http://links.lww.com/ALN/C705], 6 [http://links.lww.com/ALN/C706], 7 [http://links.lww.com/ALN/C707], 8 [http://links.lww.com/ALN/C708], 9 [http://links.lww.com/ALN/C709], 10 [http://links.lww.com/ALN/C710], 11 [http://links.lww.com/ALN/C711], 12 [http://links.lww.com/ALN/C712], 13 [http://links.lww.com/ALN/C713], 14 [http://links.lww.com/ALN/C714], 15 [http://links.lww.com/ALN/C715], 16 [http://links.lww.com/ALN/C716], and 17 [http://links.lww.com/ALN/C717]). The video bronchoscopy recordings for all 17 subjects at each phase of the staged inductions are also provided (Supplemental Digital Content 18 [http://links.lww.com/ALN/C718], 19 [http://links.lww.com/ALN/C719], 20 [http://links.lww.com/ALN/C720], 21 [http://links.lww.com/ALN/C721], 22 [http://links.lww.com/ALN/C722], 23 [http://links.lww.com/ALN/C723], 24 [http://links.lww.com/ALN/C724], 25 [http://links.lww.com/ALN/C725], 26 [http://links.lww.com/ALN/C726], 27 [http://links.lww.com/ALN/C727], 28 [http://links.lww.com/ALN/C728], 29 [http://links.lww.com/ALN/C729], 30 [http://links.lww.com/ALN/C730], 31 [http://links.lww.com/ALN/C731], 32 [http://links.lww.com/ALN/C732], 33 [http://links.lww.com/ALN/C733], and 34 [http://links.lww.com/ALN/C734]).

Discussion

This prospective observational study provides direct visual evidence of the dynamic behavior of extrinsically compressed central airways in 17 adult patients during each phase of a staged induction. Our most important finding

Table 1. Patient Characteristics

Subject	Sex	Age	BMI	FEV_1(%)	FEV_1/Forced Vital Capacity (%)	Peak Expiratory Flow Rate (l/s)
1	Male	69	24.4	—	—	—
2	Female	59	21.4	51	58	—
3	Male	22	35.5	65	83	10.6
4	Female	55	20.4	113	79	5.96
5	Female	66	23.1	78	79	3.7
6	Female	35	25.6	—	—	—
7	Female	34	23.8	73	96	4.96
8	Male	33	22.0	98	77	8.99
9	Female	64	27.0	111	98	4.52
10	Female	44	22.6	48	70	4.55
11	Male	34	26.5	65	53	—
12	Female	67	21.0	—	—	—
13	Female	78	36.2	—	—	—
14	Male	32	28.6	26	88	2.45
15	Male	61	20.0	—	—	—
16	Female	72	22.1	93	93	3.64
17	Female	56	22.0	79	65	4.06

BMI, body mass index; FEV_1, forced expiratory volume in 1 sec.

was that no statistically significant decrease in anterior–posterior diameter was observed with the introduction of general anesthesia, positive pressure ventilation, or neuromuscular blockade compared to the awake, spontaneous breathing state. Airway patency scores increased with the introduction of positive pressure ventilation and this change persisted with neuromuscular blockade. No patient suffered airway collapse or required hemodynamic or ventilatory rescue interventions.

These observations challenge prevailing physiologic concepts regarding positive pressure ventilation and use of neuromuscular blocking agents. The number and variety of mediastinal masses in this study lend weight to this finding (table 2) and have important mechanistic, and potential clinical implications. We emphasize that only adults were included in this study and that patterns of ventilation (V_T, RR, inspiratory-to-expiratory ratio, and flow- *vs.* time-pattern) were similar during the different phases of the staged induction. Hence, our conclusions may not apply to children or to situations where ventilation parameters are changed.

All patients met inclusion criteria of at least moderate airway compression based on preoperative computed tomographic scan–determined airway cross-sectional area grades of II (50% to 70% reduction in cross-sectional area) or III (more than a 70% reduction in cross-sectional area) by the Cotton–Myer method[10,11] (table 2).

Observations of airway caliber changes during the different phases of a staged induction focused on anterior–posterior diameter rather than airway cross-sectional area for two reasons. First, because extrinsic airway compression from anterior mediastinal masses takes place primarily in the anterior–posterior direction, it logically represents the more sensitive and clinically meaningful dimension. Second, there is evidence of greater reliability using anterior–posterior diameter to assess central airway compression compared to cross-sectional area.[13,14]

We employed subjective assessments of airway changes for several reasons. No standard accepted technique exists for quantitative measurements of airway stenosis by bronchoscopy.[12] Objective techniques to adjust for the bronchoscope's wide-angle lens distortions,[15–18] or for 3- to 2-dimensional conversions,[19] are complex and have not been widely validated or embraced.[12] By analogy, a 2-dimensional picture of railroad tracks stretching to the horizon depicts converging rails, but subjectively, the brain more accurately perceives the separation between rails as a constant quantity.[20] In a survey of 118 interventional pulmonologists, 91% reported using subjective visual estimation alone.[12] Interobserver variability in our study was satisfactory, and the magnitude of observed changes in anterior–posterior diameter was below what would be considered clinically significant.

Prevailing assumptions that spontaneous ventilation and intact muscle tone help preserve central airway patency extrinsically compressed by a mediastinal mass derive entirely from physiologic arguments and case reports. The vast majority of case reports involve children. All are subject to selection bias and other inherent limitations of case reports. Most predate readily available fiberoptic bronchoscopes and lack objective confirmation of central airway collapse. While some appear to support an apparent temporal association between ventilatory crises and induction, transition to positive pressure ventilation, or paralysis (or resolution with emergence and return of spontaneous ventilation),[1,21–24] that association is poor or reversed in others,[1,25–27] and often the precise timing of events is difficult to determine. More compressible, small

Table 2. Mass Characteristics

Subject	Mass Volume (mm^3)	Mass Maximal Diameter (mm)	Mediastinal Position (Relative to Airway)	Site of Maximal Stenosis	Myer–Cotton Grade of Stenosis*	Anterior–Posterior Diameter (% Reduced)	Other Invasion/ Compression	Histology
1	497	13	Anterior	Carina	II	60	Superior vena cava compression; pericardial effusion	Squamous cell carcinoma
2	1,270	13	Anterior	Left main bronchus	III	75	Superior vena cava compression; chest wall invasion	Poorly differentiated carcinoma
3	1,081	14	Anterior	Distal trachea	III	77	Superior vena cava and pulmonary artery compression	Lymphoblastic leukemia
4	289	11	Anterior	Left main bronchus	III	80	Superior vena cava compression	Thymoma
5	344	12	Anterior	Distal trachea	II	55		Thymic carcinoma
6	585	16	Anterior	Left main bronchus	III	90	Superior vena cava and pulmonary artery compression	Renal cell carcinoma
7	367	12	Anterior	Right main bronchus	II	50	Superior vena cava compression	B-cell lymphoma
8	1,654	18	Anterior	Left main bronchus	III	95	Pulmonary artery compression	Hodgkin lymphoma
9	321	12	Anterior and posterior	Distal trachea	III	75	Superior vena cava and pulmonary artery compression	B-cell lymphoma
10	620	15	Anterior and posterior	Proximal trachea	III	95		Substernal goiter
11	614	12	Anterior	Distal trachea	II	60		Liposarcoma
12	165	10	Anterior and posterior	Left main bronchus	III	95	Airway and vascular invasion	Non–small cell carcinoma
13	317	8	Anterior	Distal trachea	II	60	Pulmonary artery compression	Small cell carcinoma
14	2,970	22	Anterior	Left main bronchus	III	99		Ameloblastic carcinoma
15	112	9	Posterior	Left main bronchus	III	99		Squamous cell carcinoma
16	88	5	Anterior and posterior	Distal trachea	III	80		Non–small cell lung cancer
17	56	5	Anterior	Right main bronchus	III	85	Airway and vascular invasion; superior vena cava compression	Poorly differentiated carcinoma

*Meyer–Cotton grade of airway stenosis; see Cotton[10] and Meyer *et al.*[11]

diameter pediatric airways likely behave differently than those of the adult.

In adults with mediastinal masses, case reports of central airway obstruction are rare and do not reflect a temporal correlation with initiation of positive pressure ventilation or neuromuscular blockade. Gardner described bronchoscopically-verified airway collapse despite maintenance of spontaneous ventilation.[28] Kafrouni described the mediastinal mass–related inability to ventilate in an adult during spontaneous ventilation that improved with positive pressure ventilation.[29] Bechard retrospectively reviewed 105 anesthetics in adults with mediastinal masses, of which 97 involved general anesthesia with positive pressure ventilation and paralysis for some or all of those cases. No instances of airway collapse were observed, but seven cases of life-threatening ventilatory complications were, all of which occurred postoperatively during awake, spontaneous ventilation.[30]

Current physiologic explanations for mediastinal mass–related airway collapse during anesthesia have been thoroughly reviewed elsewhere.[1,6,7] Transitioning to the anesthetized state, with its associated decrease in functional residual capacity,[31] would be expected to exacerbate crowding and mass effects on compressible airways. Associated airway smooth muscle relaxation may also reduce resistance to compression.[1,32] We observed a minor, nonsignificant effect of induction in our study, possibly because the patients remained in the semisitting position; the supine position further reduces functional residual capacity and may have changed our results.

Substituting positive pressure for negative pressure ventilation increases mediastinal pressures[33] and may reverse the distending transpulmonary pressure gradient of spontaneous ventilation. However, the net transpulmonary pressure gradient is the sum of all incident forces. Increased intraluminal pressure may compensate for lost negative pleural pressure, and favor airway caliber preservation or even expansion. Air trapping distal to the stenotic central airway may exacerbate compressive forces. Thus, we contend that the pattern of ventilation, and its net effect on transpulmonary forces determines airway caliber changes rather than the positive or negative mode of ventilation *per se*. During positive pressure ventilation the competing effects of pneumatic stenting and dynamic hyperinflation may interact in a complex way over time, possibly explaining delayed airway collapse. We attempted to mimic the pattern of spontaneous

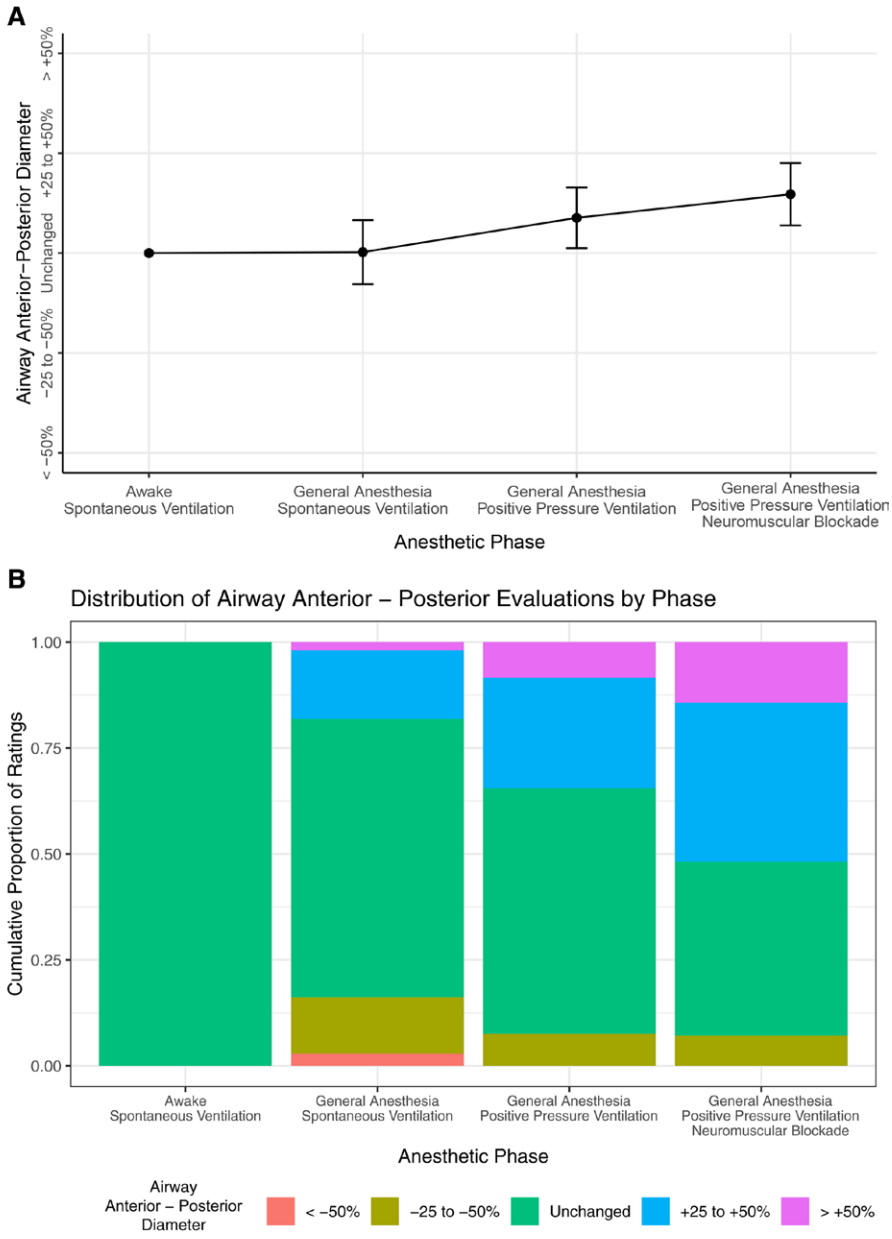

Fig. 1. (*A*) Mean airway anterior–posterior diameters according to airway patency scores (see article) during different phases of a staged anesthetic induction compared to baseline (awake, spontaneous breathing); *vertical bars* indicate 95% CI. The mean airway patency score increased significantly during the phase of positive pressure ventilation and with neuromuscular blockade, relative to that of the awake, spontaneous ventilation state. (*B*) Distribution of airway anterior–posterior evaluations by phase. The cumulative proportion of ratings are plotted for each of the anesthetic phases.

ventilation throughout in order to limit the number of changes between phases. We speculate that exacerbation of airway compression may occur if the pattern of ventilation is altered with increased V_T or inspiratory-to-expiratory ratios predisposed to air trapping distal to stenotic central airways (although this remains unproven). More severely stenotic airways would be more prone to air trapping.

The independent effect of neuromuscular blockade is difficult to separate from the preceding phase of positive pressure ventilation. It appeared that the effect of positive pressure ventilation persisted into the paralysis phase without change. We also observed a previously described[9] diminution in respiratory variation during the paralysis phase which remains unexplained.

Although we observed respiratory cycle–related movement, changes in airway caliber due to the respiratory cycle appeared to be relatively small were not technically feasible to score, and were beyond the aims and scope of this study to

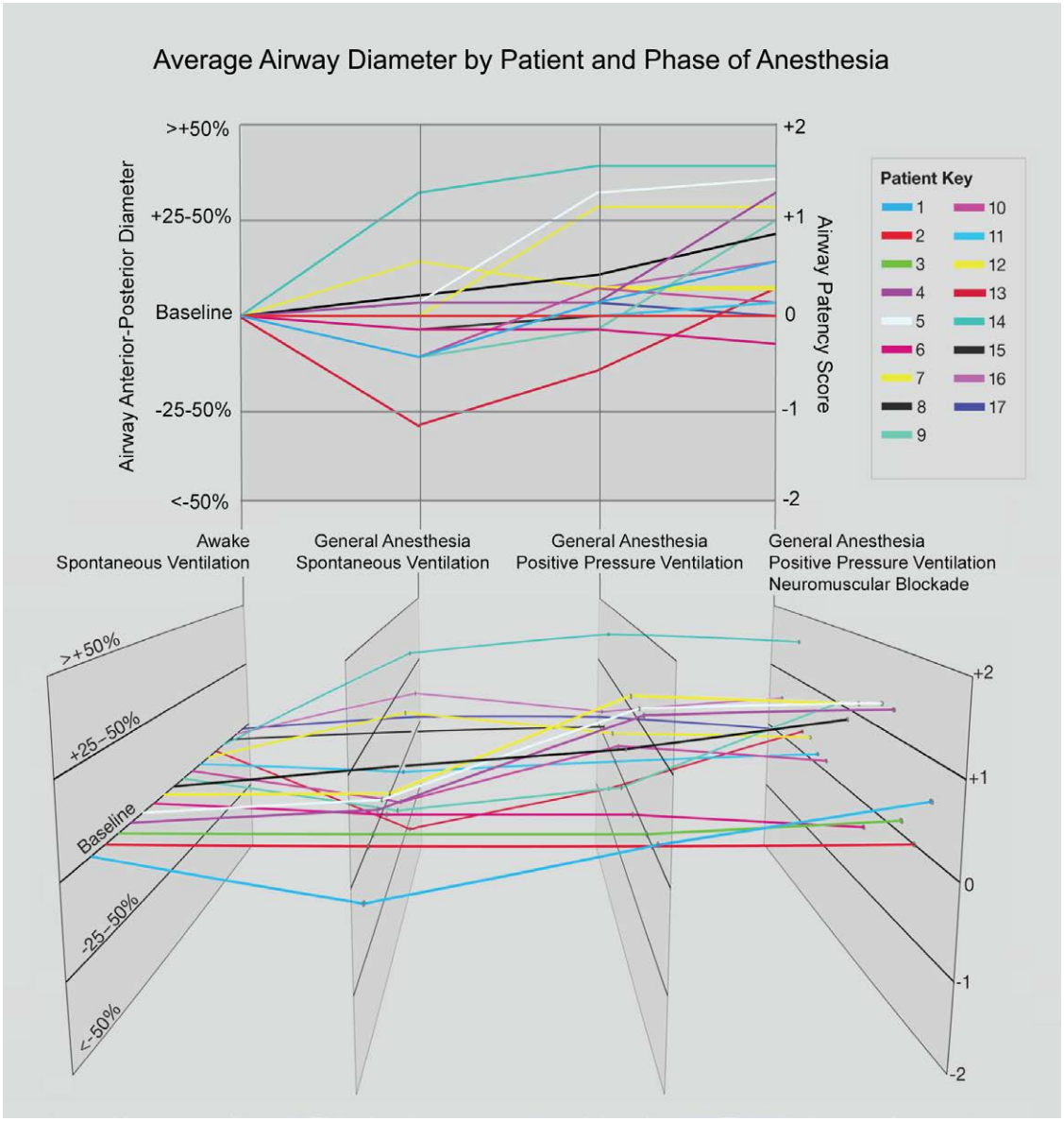

Fig. 2. *Upper panel* depicts a 2-dimensional plot of the 17 individual patients' anterior–posterior airway diameter changes according to airway patency scores (see article) during different phases of a staged anesthetic induction compared to their own baseline (awake, spontaneous breathing). *Lower panel* depicts a 3-dimensional rendition of the same data to achieve separation of individual patients, with patient no. 1 in foreground and patient no. 17 most distant. Data points at the intersection of lines with planes each represent the mean of airway patency scores from 7 observers. (Two patients [no. 8 and no. 15] had missing data points due to technical reasons, shown by a break in the line at the point of intersection with the plane representing that phase of induction.)

measure. Airway patency scoring was based on the maximal degree of airway compression irrespective of respiratory phase.

As with positive pressure during inspiration, PEEP may act as a "pneumatic stent" during the expiratory phase, and has been demonstrated to improve ventilation to lung regions previously excluded by extrinsic mainstem bronchial compression from an anterior mediastinal mass.[34] However, the effects of PEEP with obstruction are complex and difficult to predict.[35] Although extrinsic PEEP was not used in our study, some degree of intrinsic PEEP cannot be excluded. During expiration in the absence of PEEP, one would expect the effects of spontaneous and positive pressure ventilation on airway obstruction to be similar since expiration is passive in both modes.

If verified, the forgoing observations and mechanistic hypothesis will impact the rationale behind clinical practice recommendations and to a lesser extent, may influence practice. As it is more likely that dynamic

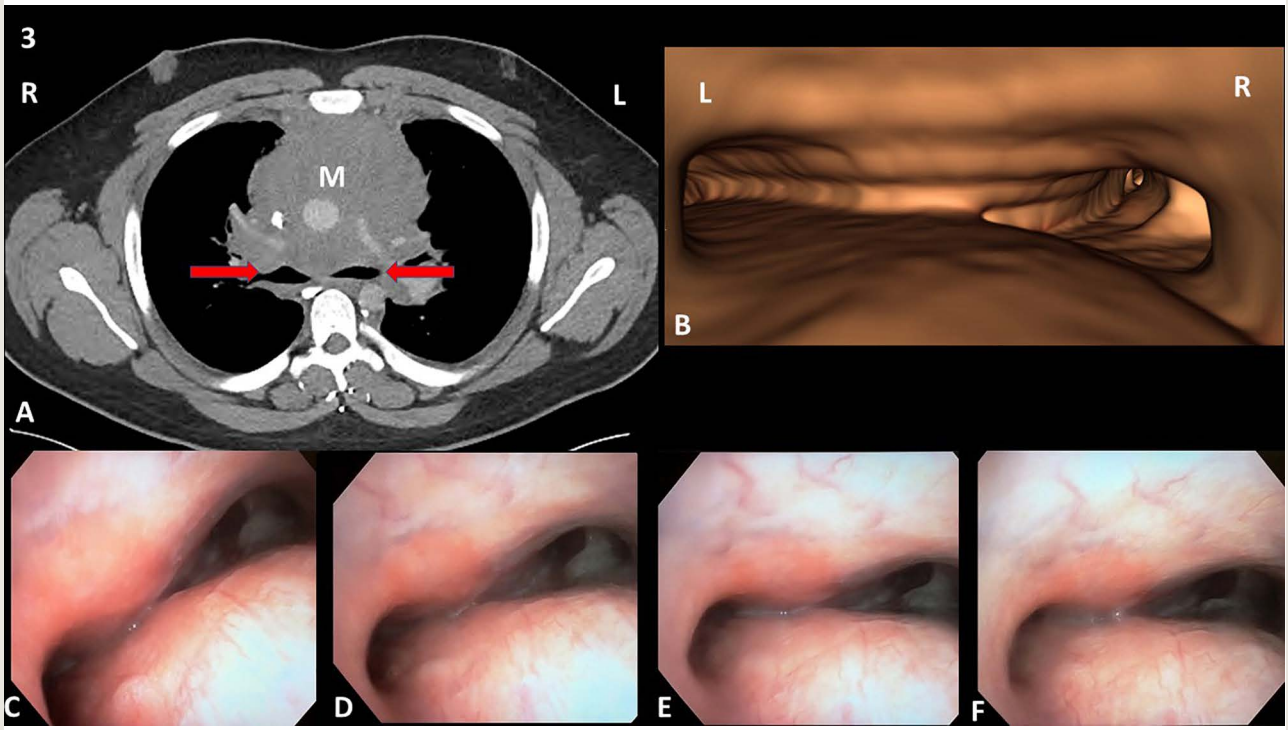

Fig. 3. (*A*) Contrast axial chest computed tomographic scan of subject no. 3 at the level of the carina demonstrating a mediastinal mass primarily anterior to the central airways. *M* indicates the mass. *Red arrows* indicate compressed mainstem bronchi. (*B*) Digital virtual bronchoscopy of the region of central airway stenosis from the same patient. (*C*) Actual bronchoscopic still picture of the central airways during baseline awake, spontaneous ventilation; (*D*) during general anesthesia maintaining spontaneous ventilation; (*E*) during general anesthesia with positive pressure ventilation; and (*F*) during general anesthesia with positive pressure ventilation and neuromuscular blockade. See Supplemental Digital Content for all 17 patients' computed tomography scans, virtual bronchoscopies, and still pictures and associated videos demonstrating clinically insignificant changes in airway patency during staged inductions.

hyperinflation will occur with positive pressure ventilation, there should remain a preference for spontaneous ventilation. However, our findings indicate that at least brief periods of similarly patterned positive pressure ventilation may safely be employed if, for example, desaturation or apnea occurs during an attempted induction of spontaneous ventilation. The staged induction protocol recommended by leading texts for patients at intermediate/indeterminant risk[36] calls for return to spontaneous breathing if ventilation difficulty occurs with positive pressure. Our findings do not reassure that such a change will reverse a collapsing airway and we would instead propose advancement of a stenting endotracheal tube. For patients deemed high risk, we advocate early intubation to provide for monitoring airway compression and if necessary, for advancing a stenting conduit.

We acknowledge several limitations. First, the number of patients was small due to the rarity of the syndrome. Second, few patients had critical airway compression and all had secured upper airways. Third, despite efforts to maintain consistent respiratory patterns across phases, breath-to-breath variation was inherent and unavoidable. Fine discrimination between end-inspiration and end-expiration airway diameters was not technically feasible. Fourth, the duration of observation for each phase was relatively brief and we are unable to confirm that prolonged positive pressure ventilation or neuromuscular blockade would have changed our results. Fifth, assessments of anterior–posterior diameter changes were based on subjective assessments as previously explained. However, the precise magnitude of airway diameter changes is less important than the finding that the direction of change with positive pressure ventilation is in opposition to predictions based on prevailing assumptions.

In conclusion, we observed no worsening of central airway compression in adults with large mediastinal masses when induction, positive pressure ventilation, and paralysis were introduced in a staged manner. This suggests a need to reexamine presumed mechanisms of airway collapse during anesthesia in such patients. Our observations may only apply to the specific staged protocol described (including semisitting posture and maintaining ventilation patterns tolerated during spontaneous breathing). We emphasize that our findings do not prove that conventional (nonstaged) inductions are safe for this population, which is also at risk of hemodynamic collapse.

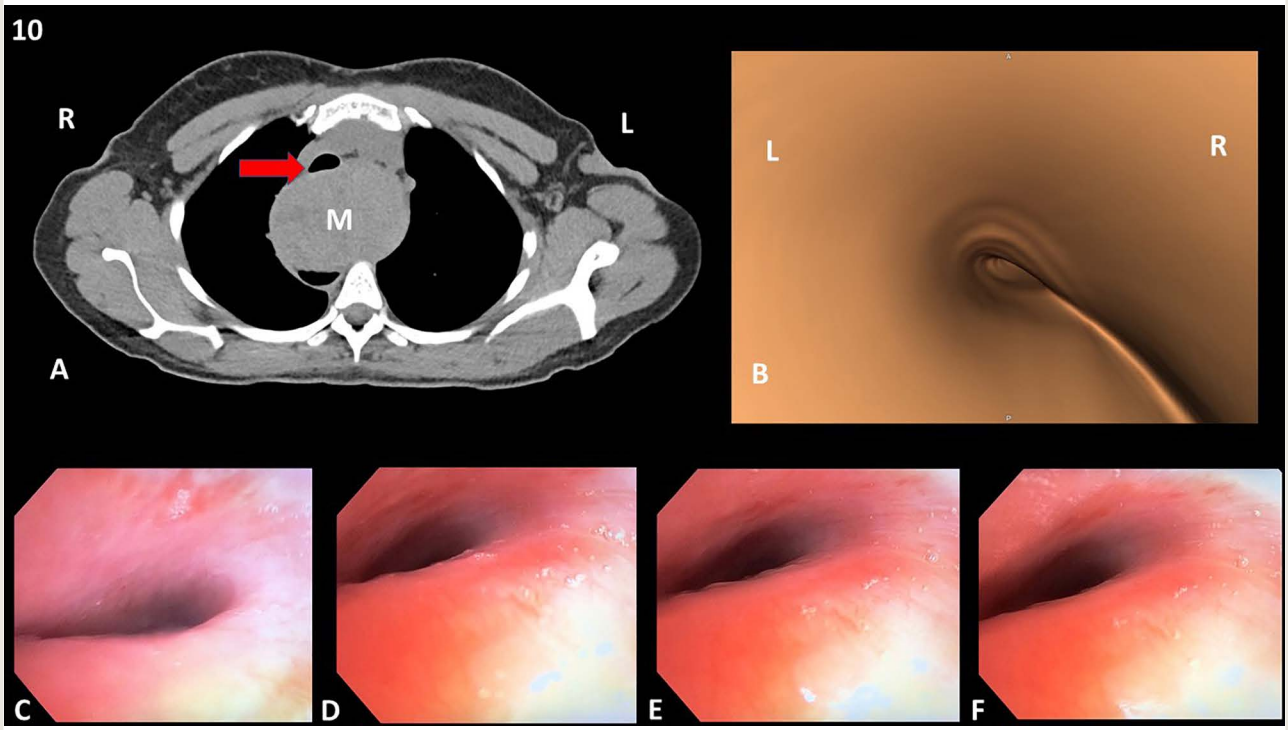

Fig. 4. (*A*) Contrast axial chest computed tomographic scan of subject no. 10 demonstrating a mediastinal mass primarily posterior to the central airway. *M* indicates the mass. *Red arrow* indicates compressed trachea. (*B*) Digital virtual bronchoscopy of the region of central airway stenosis from the same patient. (*C*) Actual bronchoscopic still picture of the central airway during baseline awake, and spontaneous ventilation; (*D*) during general anesthesia maintaining spontaneous ventilation; (*E*) during general anesthesia with positive pressure ventilation; and (*F*) during general anesthesia with positive pressure ventilation and neuromuscular blockade. See Supplemental Digital Content for all 17 patients' computed tomography scans, virtual bronchoscopies, and still pictures and associated videos demonstrating clinically insignificant changes in airway patency during staged inductions.

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Competing Interests

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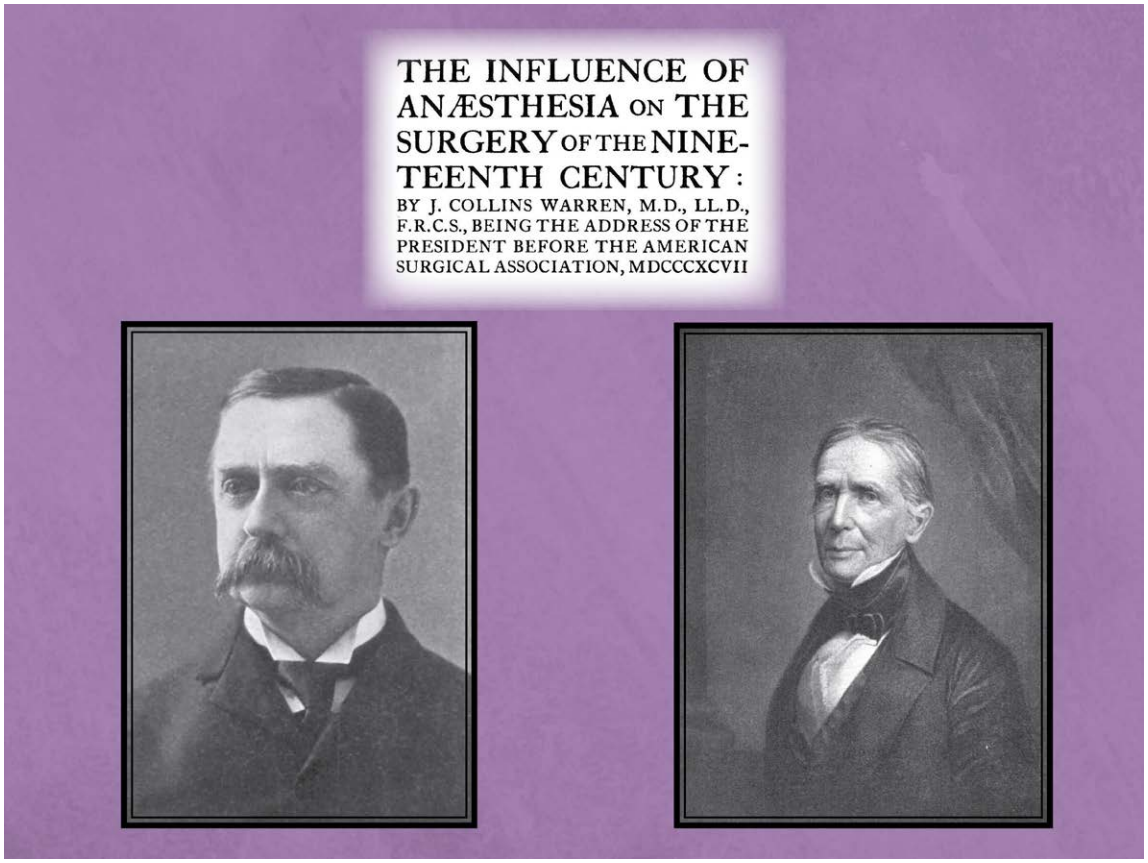
No Humbug Here—Celebrating Ether Day in the Spirit of J. C. Warren



For the fiftieth anniversary of Ether Day, J. Collins Warren addressed the American Surgical Association in 1897 about the "Influence of Anaesthesia on the Surgery of the Nineteenth Century." At first glance, it may appear that the attending surgeon from October 16, 1846, John Collins Warren, M.D. (*bottom right*), was posthumously presenting a spirited speech four decades after his death. Upon closer inspection, the reader learns that J. Collins Warren, M.D. (*bottom left*), the grandson of the elder Dr. Warren, is reflecting on his family legacy and reminding fellow surgeons that surgical advancement should "excite our industry rather than our vanity." Though it is debatable whether the senior Dr. Warren truly uttered the famous phrase "Gentlemen! This is no Humbug," the Warren family's dedication to painless surgery is not in question. The elder Warren did advocate ether administration during surgery and wrote several papers and books to encourage etherization. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology. www.woodlibrarymuseum.org)

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