ANESTHESIOLOGY

Mechanical Power during General Anesthesia and Postoperative Respiratory Failure: A Multicenter Retrospective Cohort Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- The concept of mechanical power during ventilation integrates inspiratory and positive end-expiratory pressures, tidal volume, and respiratory rate into a single calculated quantity
- Higher mechanical power during ventilation is associated with mortality and lung injury in the critical care setting
- It is unclear whether mechanical power during intraoperative mechanical ventilation is associated with adverse outcomes

What This Article Tells Us That Is New

- Among 230,767 elective surgery patients across two medical centers, the median mechanical power was 6.63 J/min, and 2,024 patients (0.9%) required reintubation within 7 days
- Patients experiencing reintubation within 7 days after surgery had a higher median mechanical power (7.67 [5.64 to 10.11] *vs.* 6.62 [4.62 to 9.10] J/min; $P < 0.001$)
- For each 5-J/min rise in intraoperative mechanical power, the adjusted risk of reintubation was 31% higher

ABSTRACT

Background: Mechanical power during ventilation estimates the energy delivered to the respiratory system through integrating inspiratory pressures, tidal volume, and respiratory rate into a single value. It has been linked to lung injury and mortality in the acute respiratory distress syndrome, but little evidence exists regarding whether the concept relates to lung injury in patients with healthy lungs. This study hypothesized that higher mechanical power is associated with greater postoperative respiratory failure requiring reintubation in patients undergoing general anesthesia.

Methods: In this multicenter, retrospective study, 230,767 elective, noncardiac adult surgical out- and inpatients undergoing general anesthesia between 2008 and 2018 at two academic hospital networks in Boston, Massachusetts, were included. The risk-adjusted association between the median intraoperative mechanical power, calculated from median values of tidal volume (V_t), respiratory rate (RR), positive end-expiratory pressure (PEEP), plateau pressure (P_{plat}), and peak inspiratory pressure (P_{peak}), using the following formula: mechanical power (J/min) = $0.098 \times RR \times V_t \times (PEEP + ½[P_{plat} - PEEP] + [P_{peak} - P_{plat}])$, and postoperative respiratory failure requiring reintubation within 7 days, was assessed.

Results: The median intraoperative mechanical power was 6.63 (interquartile range, 4.62 to 9.11) J/min. Postoperative respiratory failure occurred in 2,024 (0.9%) patients. The median (interquartile range) intraoperative mechanical power was higher in patients with postoperative respiratory failure than in patients without (7.67 [5.64 to 10.11] *vs.* 6.62 [4.62 to 9.10] J/min; $P < 0.001$). In adjusted analyses, a higher mechanical power was associated with greater odds of postoperative respiratory failure (adjusted odds ratio, 1.31 per 5 J/min increase; 95% CI, 1.21 to 1.42; $P < 0.001$). The association between mechanical power and postoperative respiratory failure was robust to additional adjustment for known drivers of ventilator-induced lung injury, including tidal volume, driving pressure, and respiratory rate, and driven by the dynamic elastic component (adjusted odds ratio, 1.35 per 5 J/min; 95% CI, 1.05 to 1.73; $P = 0.02$).

Conclusions: Higher mechanical power during ventilation is statistically associated with a greater risk of postoperative respiratory failure requiring reintubation.

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Postoperative pulmonary complications occur in about 1 million patients each year in the United States alone and are responsible for an estimated 46,200 deaths and 4.8 million days of hospitalization.[1] These life-threatening events predispose to respiratory failure and reintubation with subsequent, unplanned intensive care unit admission and are associated with a 9-fold increase in postoperative mortality[2,3] and increased economic burden to healthcare systems.[1]

Previous studies have focused on intraoperative lung-protective ventilation to prevent postoperative pulmonary complications but have yielded equivocal results:

This article is featured in "This Month in Anesthesiology," page A1. This article is accompanied by an editorial on p. 6. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has an audio podcast. This article has a visual abstract available in the online version. Preliminary results of this study were presented as an abstract at the Association of University Anesthesiologists Annual Meeting in Toronto, Ontario, Canada, May 12 and 13, 2021, and an abstract focusing on the effects of temporal changes of mechanical power was presented at the American Society of Anesthesiologists Annual Meeting in San Diego, California, October 9 to 13, 2021.

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the combination of lowering tidal volume and applying positive end-expiratory pressure, which resulted in lower driving pressures, improved postoperative pulmonary function[4] and reduced major postoperative adverse events.[5] Trials investigating single interventions were, however, nonconfirmatory: a recent, single-center randomized controlled trial failed to demonstrate an effect of low (6 ml/kg) *versus* high tidal volumes (10 ml/kg) in patients undergoing surgery,[6] reflecting previous, smaller trials.[7] While tidal volume was the only randomized variable in these studies, there was an associated increase in respiratory rate, potentially offsetting the beneficial effect of lowering tidal volume.[8,9] This illustrates the need for a unifying concept that integrates the effects of changes in multiple parameters when adjusting mechanical ventilation to reduce perioperative ventilator-induced lung injury.

Mechanical power is a concept novel to mechanical ventilation that estimates the energy delivered to the respiratory system and the lung during mechanical ventilation in joules per minute (J/min).[10–14] While mechanical power is ideally calculated from continuous recordings of pressure and flow, an abbreviated formula based on routine clinical data has been validated.[11] The concept integrates ventilator-delivered inspiratory work, calculated from inspiratory pressures and tidal volume, and cyclic repetition, derived from respiratory rate.[15] It further allows physicians to assess adjustments to mechanical ventilation by calculating a single value. A *post hoc* analysis[16] of the aforementioned randomized controlled trial[6] conducted in response to an accompanying letter[9] found that while there was no effect of low *versus* high tidal volumes, a higher mechanical power during ventilation was associated with a greater risk of postoperative pulmonary complications.

Retrospective studies in mechanically ventilated patients suffering from acute respiratory distress syndrome (ARDS) reported a greater mortality when a higher mechanical power was applied.[17–19] However, its role in the development of respiratory failure in patients without lung injury is poorly understood. It is unclear whether the evidence from patients with ARDS is translatable to patients undergoing general anesthesia, which typically show fundamentally different pulmonary mechanics and a higher lung volume available for aeration.

In this study, we hypothesized that higher mechanical power applied during intraoperative mechanical ventilation is associated with postoperative respiratory failure requiring reintubation. We further investigated whether this concept adds information in addition to established parameters implicated in ventilator-induced lung injury during intraoperative mechanical ventilation.

Materials and Methods

Study Design

This retrospective cohort study analyzed data from surgical cases performed between 2008 and 2018 at two academic hospitals: Massachusetts General Hospital and Beth Israel Deaconess Medical Center in Boston, Massachusetts. The study was reviewed by the institutional review boards at both institutions, which determined that it met the criteria for exempt status (protocol Nos. 2020P003633 and 2020P001072). The requirement for informed consent was waived. A data analysis and statistical plan was established before the data were accessed. Changes and additions to the statistical analysis plan were documented and are provided in the Supplemental Digital Content together with the institutional review board approval (Supplemental Digital Content 1, http://links.lww.com/ALN/C854). The data were extracted from electronic medical records, including minute-by-minute recordings of ventilator parameters, as described in section S1 of Supplemental Digital Content 2 (http://links.lww.com/ALN/C855).

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Patient Selection

Adult patients undergoing general anesthesia for noncardiac surgical procedures with available electronic documentation of exposure, primary outcome, and airway device were considered for inclusion. Both in- and outpatients were included. Patients with an American Society of Anesthesiologists physical status classification greater than or equal to V and patients undergoing emergency surgery were excluded. Cases with missing data for confounder variables were excluded, and analyses were performed using the complete-case approach.

Exposure

The primary exposure was defined as the intraoperative mechanical power during ventilation estimated from median values of tidal volume (V_t), respiratory rate (RR), positive end-expiratory pressure (PEEP), plateau pressure (P_{plat}), and peak inspiratory pressure (P_{peak}) during intraoperative mechanical ventilation. Mechanical power was calculated using a validated method[11,17,19] consisting of an abbreviated formula developed for use in epidemiologic studies.[11] The formula was previously expressed as follows: mechanical power (J/min) = $0.098 \times RR \times V_t \times (PEEP + ½[P_{plat} - PEEP] + [P_{peak} - P_{plat}])$.[19] Thus, mechanical power is calculated from the work of breathing for individual breaths (volume × pressure product) multiplied by the respiratory rate.[15] The formula further illustrates the static (PEEP), dynamic elastic (P_{plat} − PEEP), and dynamic resistive ($P_{peak} - P_{plat}$) components of work of breathing and mechanical power (fig. 1), which were calculated separately. For patients with missing plateau pressure, peak inspiratory pressure was used as surrogate, and a sensitivity analysis was conducted in patients with available plateau pressures.

Primary and Secondary Outcomes

The primary outcome was postoperative respiratory failure requiring reintubation within 7 days. The secondary outcome was postextubation hypoxemia, defined as peripheral oxygen saturation (Spo_2) of less than 90% within 10 min of extubation or until departure from the operating room.

Primary Analysis

In the primary analysis, we assessed the association between intraoperative mechanical power and postoperative

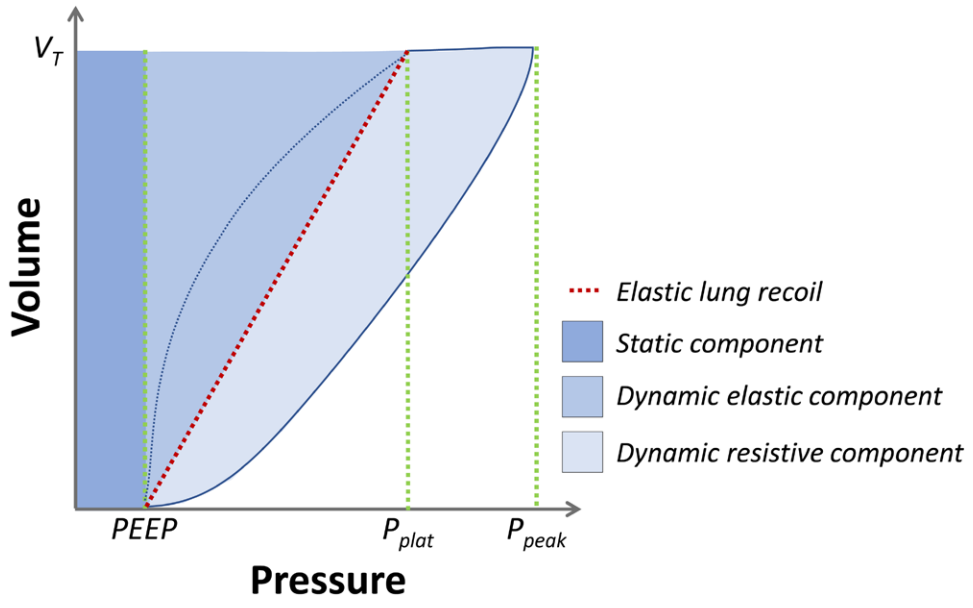


Fig. 1. Concept and components of mechanical power: exemplary pressure–volume loop of a single breath in a passive patient during general anesthesia. Mechanical power (in joules per minute) is derived from the mechanical work of single breaths and respiratory rate. The work of breathing is represented by the area under the inspiratory limb of the pressure–volume curve (*solid blue line*) and has three components: a static component generated by positive end-expiratory pressure (PEEP; shown as *dark blue shading*); a *dynamic elastic* component (shown as *medium blue shading*) that reflects mechanical power to overcome the elastic recoil of the respiratory system (*red dotted line*); and a *dynamic resistive* component to overcome airway resistance (shown as *light blue shading*). The expiratory limb (*dotted blue line*) of the pressure–volume curve is not incorporated into the calculation of mechanical power. While mechanical power is ideally calculated from continuous recordings of airway pressure and flow, a simplified equation has been validated for use in epidemiologic studies: mechanical power = $0.098 \times$ respiratory rate × tidal volume × (PEEP + $0.5 \times (P_{plat} - PEEP) \times (P_{peak} - P_{plat})$), where P_{plat} is the plateau pressure, and P_{peak} is the peak pressure. The static, dynamic elastic, and dynamic resistive components are approximated by the PEEP, $0.5 \times (P_{plat} - PEEP)$, and $(P_{peak} - P_{plat})$ part of the equation, respectively.

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respiratory failure requiring reintubation within 7 days[8,20] after surgery using mixed-effects multivariable logistic regression (model 1). Postoperative reintubation was defined based on billing data provided by respiratory therapists[8,20–22] and cross-validated using International Classification of Diseases (9th and 10th Revision, Clinical Modification) diagnostic codes (96.01, 96.02, 96.03, 96.04, 96.05, 0BH17EZ, and 0BH18EZ), Current Procedural Terminology codes (31500), and chart reviews in randomly selected patients. Analyses were adjusted for *a priori* defined confounders based on existing literature and clinical plausibility.[8,20,22,23] Patient-specific confounders included age, sex, body mass index, American Society of Anesthesiologists physical status, Charlson Comorbidity Index,[24] high risk of postoperative pulmonary complications (defined as a score for prediction of postoperative respiratory complications [SPORC] greater than or equal to 7),[25] history of smoking, and diagnoses of heart failure or chronic obstructive pulmonary disease within 1 yr before surgery. Procedure-related confounders included surgical service, duration of surgery, work relative value units as a marker for the procedural complexity based on Current Procedural Terminology codes, duration of intraoperative hypotension (*i.e.*, time with mean arterial pressure less than 55 mmHg),[26] norepinephrine-equivalent vasopressor dose,[27] administered intravenous fluid volume, packed erythrocyte units, morphine-equivalent doses of short- and long-acting opioids,[28,29] nondepolarizing neuromuscular blocking agent dose (expressed as ED_{95} equivalent doses),[30] weight-adjusted neostigmine dose (μg/kg), the use of sugammadex, age-adjusted minimum alveolar concentration of inhalational anesthetics, fraction of inspired oxygen (FIO_2), and airway device (*i.e.*, endotracheal tube *vs.* laryngeal mask airway). To account for the period over which data were collected, we adjusted our analyses also for the year of surgery. The study site was included as a random effect to the mixed effects model to account for the multicenter design. Detailed information on all confounders and the random effect are provided in Supplemental Digital Content 2 (section S1, supplemental methods, http://links.lww.com/ALN/C855).

Statistical Analyses

Statistical analyses, study endpoints, and confounding variables were defined *a priori* before accessing data for analyses. Multivariable mixed-effects logistic regression analyses were performed to evaluate relationships between intraoperative median mechanical power and primary and secondary outcomes. Adjusted odds ratios and 95% CI are presented for multivariable logistic regression models. For the mixed-effects regression model, we extended the model by adding the study center as a random effect to the model, nesting anesthesia providers in their respective hospitals, as previously published.[31] The primary regression model was conducted using forced variable entry and evaluated to ensure that the estimations could be interpreted conventionally. Model calibration of the primary analysis was evaluated through a reliability plot (Supplemental Digital Content 1, fig. S1, http://links.lww.com/ALN/C855), and this evaluation indicated an acceptable fit. Model discrimination was assessed through the concordance c-statistic, which in our case was equivalent to the area under the receiver operating characteristic curve. The area under the receiver operating characteristic curve was 0.86, indicating excellent model discrimination. The association of continuous variables with the primary outcome was assessed for linearity; in case of nonlinearity, continuous confounders were categorized into quintiles or clinically relevant categories. Continuous variables were compared using unpaired Student's *t* test or Mann–Whitney U test, as appropriate. In cases with available minute-by-minute ventilator data, mechanical power derived from medians was compared to mechanical power based on minute-by-minute data by means of Bland–Altman analysis (Supplemental Digital Content 2, section S2, sensitivity analyses; and fig. S2, http://links.lww.com/ALN/C855). Statistical significance was assumed at $P < 0.05$. Analyses were performed using Stata (version 15.1, StataCorp LLC, USA) and R Statistical Software (Foundation for Statistical Computing, Austria).

Secondary Analyses

In secondary analyses, we evaluated the association between intraoperative mechanical power and postextubation hypoxemia, which has been associated with poor patient outcome and increased level of hospitalization.[32] This analysis was done using the same mixed-effects multivariable regression model as for the primary analysis. Postextubation hypoxemia was defined as SpO_2 of less than 90% within 10 min of extubation or until departure from the operating room. Stored SpO_2 values averaged over 1-min intervals were accessed for this analysis. Any measurement of 0% was set to missing.

In an alternative statistical model (model 2), we additionally adjusted the association between mechanical power and the primary outcome for known drivers of ventilator-induced lung injury, including tidal volume,[5] driving pressure,[33] and respiratory rate[8] to assess whether the concept of mechanical power adds additional information to its individual components. We then explored the individual associations of the static ($V_t \times RR \times PEEP$), dynamic elastic ($V_t \times RR \times ½[P_{plat} - PEEP]$), and dynamic resistive ($V_t \times RR \times [P_{peak} - P_{plat}]$) components of mechanical power with postoperative respiratory failure by incorporating them as separate variables into the regression model (model 3).

Sensitivity Analyses

We conducted multiple sensitivity analyses to confirm robustness of the primary study findings: (1) to address a potential nonlinear relationship, we redefined the exposure by categorizing mechanical power into quintiles; (2) we

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adjusted mechanical power for ideal body weight[18,19] and body mass index[34] and repeated the primary analysis; (3) in a subgroup of patients with available minute-by-minute ventilator data, we redefined the exposure variable by calculating mechanical power on a minute-by-minute basis; (4) we repeated the primary analysis in the subgroup of patients with available plateau pressure measurements; (5) we excluded patients receiving laryngeal mask airways to test whether our results remain robust; (6) we excluded patients undergoing laparoscopic or thoracic surgeries to test whether our results remain robust; (7) we conducted subgroup analyses in inpatients with duration of surgery of 3 h or longer to test the robustness of findings in this high risk group, as well as thoracic surgery cases; (8) in a subgroup with available arterial blood gas analyses, we adjusted the primary analysis for arterial carbon dioxide partial pressure ($Paco_2$), arterial oxygen partial pressure to inspiratory oxygen fraction (Pao_2/Fio_2) ratio, and $Paco_2$ to end-tidal carbon dioxide ($Petco_2$) gradient as a marker of the degree of physiologic dead space; (9) we excluded patients who received blood transfusion during surgery to test whether our results remain significant in patients without transfusion; (10) we investigated the variability of the effect of anesthesia provider on the value of mechanical power during surgery[31]; (11) to address missing confounder data, we performed multiple imputation for any variable with missing data and repeated the primary analysis in the imputed cohort; (12) we conducted bootstrapping for our primary model; and (13) we tested the robustness using inverse probability of treatment weighting. Details on sensitivity analyses are provided in Supplemental Digital Content 2 (section S2, sensitivity analyses, http://links.lww.com/ALN/C855).

Exploratory Analyses

We evaluated changes in mechanical power during surgery by comparing the temporal trends of mechanical power between patients with and without postoperative respiratory failure requiring reintubation. A linear mixed-effects model including an interaction term between group (patients with and without respiratory failure) and time after start of anesthesia (defined by intubation time) was applied. We then investigated the association between temporal changes in mechanical power from the start to the end of surgery and the primary outcome and assessed potential cutoffs for harmful effects.

We also conducted multiple exploratory analyses to expand knowledge on exposure–outcome association: (1) we investigated the effect of intraoperative fluid administration on temporal increases of mechanical power; (2) we investigated the characteristics of exposure and outcome per year of surgery; (3) we investigated the association between mechanical power and early (postoperative days 0 to 3) *versus* late (postoperative days 4 to 7) reintubation after surgery; (4) we investigated the commonly used composite outcome of postoperative pulmonary complications, defined as atelectasis, pneumonia, respiratory failure, and exacerbation of underlying chronic lung disease[35]; (5) we conducted effect modification analysis by the depth of neuromuscular blocking; (6) we conducted effect modification analysis by the mode of ventilation, categorized into pressure control ventilation *versus* other modes of ventilation; and finally, (7) we conducted effect modification analysis by the most prominently imbalanced confounding variables. Details on exploratory analyses are added to Supplemental Digital Content 2 (section S3, exploratory analyses, http://links.lww.com/ALN/C855).

Results

Study Cohort and Characteristics

In total, 262,723 surgical cases undergoing general anesthesia between 2008 and 2018 were identified after applying inclusion criteria, of which 21,496 observations were not included due to missing exposure data. After application of exclusion criteria and excluding cases and cases with missing confounder information, the final study cohort consisted of 230,767 patients (fig. 2). The mean (SD) and median (interquartile range) mechanical power during general anesthesia were 7.1 (3.5) J/min and 6.63 (4.62 to 9.11) J/min, respectively. The distribution of intraoperative mechanical power is shown in figure 3. Baseline characteristics of the study population are provided in table 1.

Primary Analysis

In total, 2,024 (0.9%) cases required reintubation for respiratory failure within 7 postoperative days. The median (interquartile range) intraoperative mechanical power was higher in patients with postoperative respiratory failure than in patients without (7.67 [5.64 to 10.11] *vs.* 6.62 [4.62 to 9.10] J/min; $P < 0.001$). After adjustment for *a priori* defined confounders (model 1), a higher mechanical power was associated with greater odds of postoperative reintubation: with each 5-J/min increase in mechanical power, the odds of reintubation were 31% greater (adjusted odds ratio, 1.31; 95% CI, 1.21 to 1.42; $P < 0.001$; fig. 4A), corresponding to an adjusted risk of 0.8% (95% CI, 0.7 to 0.8), 1.0% (95% CI, 0.9 to 1.0), and 1.3% (95% CI, 1.1 to 1.4) in patients who received a mechanical power of 5, 10, or 15 J/min, respectively.

Secondary Analyses

Postoperative Spo_2 data were available for 179,673 patients. On average, two Spo_2 recordings for each patient were available. Each single recording reflected the average Spo_2 more than 1 min taken from 4 readings at 15-s intervals. Postextubation hypoxemia occurred in 8,374 (4.7%) patients. Greater odds of postextubation hypoxemia were associated with higher mechanical power (adjusted odds ratio, 1.26 per

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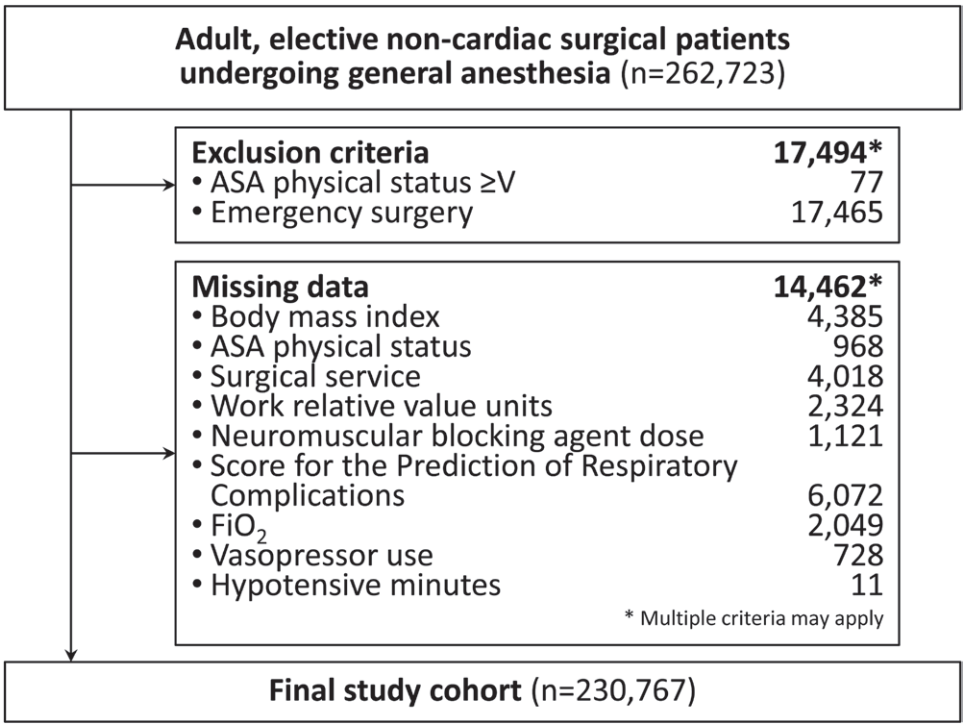


Fig. 2. Study flow diagram indicating numbers of patients excluded due to exclusion criteria and missing data in 262,723 included patients with complete data for the primary outcome and exposure. ASA, American Society of Anesthesiologists; FIO_2, fraction of inspired oxygen.

5 J/min; 95% CI, 1.21 to 1.31; $P < 0.001$), resulting in a 26% greater risk per 5-J/min increase in mechanical power.

When additionally adjusting for known drivers of ventilator-induced lung injury, including tidal volume, driving pressure, and respiratory rate (model 2), mechanical power remained independently associated with postoperative respiratory failure requiring reintubation (adjusted odds ratio, 1.22; 95% CI, 1.08 to 1.37; $P = 0.001$; fig. 4B). Dissecting mechanical power into its static, dynamic elastic, and dynamic resistive components (model 3) revealed that only the dynamic elastic component was associated with postoperative respiratory failure requiring reintubation (adjusted odds ratio, 1.35 per 5 J/min; 95% CI, 1.05 to 1.73; $P = 0.02$), while the other components showed no significant association (fig. 4B).

Sensitivity and Exploratory Analyses

In patients within the lowest quintile of mechanical power (less than 4.16 J/min), the adjusted risk of reintubation was 0.7% (95% CI, 0.6 to 0.8), as opposed to 1.1% (1.0 to 1.2) in patients within the highest quintile (greater than 9.83 J/min; adjusted risk difference, 0.4% [0.3 to 0.6]). The ranges of mechanical power for the second, third, and fourth quintiles were 4.16 to 5.84, 5.84 to 7.49, and 7.49 to 9.83 J/min, respectively.

In a hypothesis-generating exploratory analysis, there was a different temporal pattern in the intraoperative trend of mechanical power between patients with and without postoperative respiratory failure that was characterized by a constant linear increase in the former group, while no such pattern was present in the latter group ($P < 0.001$; fig. 5A). In adjusted analyses, a threshold increase in mechanical power greater than 2 J/min between start and end of surgery was significantly associated with greater risk of postoperative respiratory failure requiring reintubation, with higher thresholds showing a further risk increase (fig. 5B; Supplemental Digital Content 2, table S4, http://links.lww.com/ALN/C855). In cases exhibiting increases of greater than 2 J/min, the increase in mechanical power was driven by higher respiratory rate and driving pressure (Supplemental Digital Content 2, table S5, http://links.lww.com/ALN/C855).

Results of the primary analysis remained robust throughout multiple sensitivity analyses, which are detailed in Supplemental Digital Content 2 (section S2, sensitivity analyses, http://links.lww.com/ALN/C855). We also conducted several other exploratory analyses as previously mentioned, which are detailed in Supplemental Digital Content 2 (section S3, exploratory analyses, http://links.lww.com/ALN/C855).

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Table 1. Patient Characteristics and Distribution of Variables according to Outcome

Characteristics	No Reintubation (N = 228,743)	Reintubation (N = 2,024)
Age, yr	54 ± 16	63 ± 15
Sex, female	129,165 (56.5%)	957 (47.3%)
Body mass index	28.5 ± 6.8	28.6 ± 7.5
ASA physical status	II (II–III)	III (III–III)
Duration of surgery, min	130 (85–201)	201 (133–313)
Type of surgery		
Acute care surgery	6,690 (2.9%)	114 (5.6%)
General surgery	35,676 (15.6%)	226 (11.2%)
Gynecology	24,489 (10.7%)	46 (2.3%)
Neurosurgery	15,019 (6.6%)	247 (12.2%)
Oral/maxillofacial surgery	2,195 (1.0%)	14 (0.7%)
Orthopedic surgery	52,296 (22.9%)	475 (23.5%)
Otolaryngology	6,712 (2.9%)	17 (0.8%)
Plastic surgery	16,011 (7.0%)	45 (2.2%)
Surgical oncology	11,175 (4.9%)	49 (2.4%)
Thoracic surgery	13,580 (5.9%)	296 (14.6%)
Transplant	4,021 (1.8%)	72 (3.6%)
Urology	19,887 (8.7%)	66 (3.3%)
Vascular surgery	8,173 (3.6%)	220 (10.9%)
Other	12,819 (5.6%)	137 (6.8%)
Work relative value, units	12.6 (7.1–19.6)	20.7 (13.1–26.6)
Hypotension less than 55 mmHg, min	0.0 (0.0–3.0)	2.0 (0.0–6.0)
Total vasopressor dose, mg	0.0 (0.0–0.1)	0.2 (0.0–0.7)
Packed red blood cells, units	0 (0–0)	0 (0–0)
Fluids, ml	1,000 (700–1,650)	1,540 (1,000–2,800)
Short acting opioids, mg	37.5 (25.0–62.5)	62.5 (25.0–75.0)
Long acting opioids, mg	6.8 (0.0–17.0)	8.5 (0.0–23.8)
Nondepolarizing neuromuscular blocking agents ED95 dose, mg*	1.8 (0.0–2.9)	2.7 (1.4–4.3)
MAC of volatile agents and nitrous oxide	1.0 (0.8–1.1)	0.9 (0.7–1.1)
Neostigmine dose, μg/kg	18 (0–41)	31 (0–49)
Sugammadex dose, mg	0 (0–0)	0 (0–0)
Charlson comorbidity index	1.0 (0.0–2.0)	3.0 (1.0–6.0)
Score for prediction of postoperative respiratory complications	2.0 (0.0–3.0)	5.0 (3.0–5.0)
COPD	10,180 (4.5%)	288 (14.2%)
Congestive heart failure	12,170 (5.3%)	414 (20.5%)
Smoking	22,291 (9.7%)	276 (13.6%)
Airway device		
Endotracheal tube	188,027 (82.2%)	1,953 (96.5%)
Laryngeal mask airway	40,121 (17.5%)	63 (3.1%)
Combined	595 (0.3%)	8 (0.4%)

The data are expressed as the frequency (prevalence in %), mean ± SD, or median (interquartile range [25th to 75th percentile]).

*ED95 dose of neuromuscular blocking agents: median effective dose required to achieve a 95% reduction in maximal twitch response from baseline.

ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; MAC, minimal alveolar concentration.

Discussion

A higher mechanical power during intraoperative mechanical ventilation was statistically associated with a greater risk of postoperative respiratory failure requiring reintubation. The association between mechanical power and postoperative respiratory failure remained robust after adjusting for tidal volume, respiratory rate, and driving pressure. Of the individual components of mechanical power, only the dynamic elastic component was individually associated with postoperative respiratory failure.

In patients suffering from ARDS, a higher mechanical power has been associated with fewer ventilator-free days, longer duration of stay in the intensive care unit, and greater in-hospital mortality.[17] These findings were confirmed in secondary analyses of prospective data from patients enrolled in eight randomized, controlled trials[18] and another analysis of pooled data from six randomized, controlled trials.[19] Our results transfer these observations to patients undergoing intraoperative mechanical ventilation and suggest that the concept of mechanical power carries clinical merit by identifying patients at risk of adverse outcomes even without preexisting respiratory failure.

We observed an increase in the odds of postoperative reintubation by 1.31 per 5-J/min increase in mechanical power. In a hypothetical clinical scenario, in which a tidal

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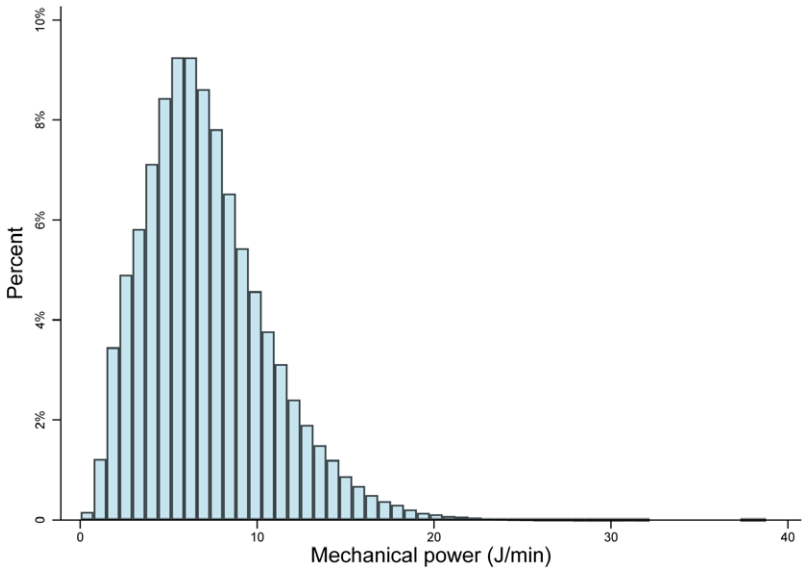


Fig. 3. Histogram depicting distribution of intraoperative mechanical power. The mean (SD) and median (interquartile range) mechanical power during general anesthesia in the study cohort was 7.1 (3.5) J/min and 6.6 (4.6 to 9.1) J/min, respectively.

volume of 6 ml/kg is administered to a 70-kg patient (static compliance, 60 ml/cm H_2O) at a respiratory rate of 10, with PEEP set to 7, a plateau pressure of 14, and a peak pressure of 17 cm H_2O, the mechanical power would be 5.6 J/min, and the adjusted absolute risk of postoperative reintubation would be 0.8%. If the respiratory rate for this patient is increased to 15 breaths/min, and the tidal volume is increased to 8 ml/kg, mechanical power will increase to 12.1 J/min, with an adjusted absolute risk of 1.1%. Based on our findings, this would be associated with a 32% greater risk for postoperative reintubation.

In our study, the average mechanical power was 7 J/min, compared to 20 to 30 J/min in critically ill patients.[15] Compared to patients suffering from ARDS, patients undergoing general anesthesia for elective surgery typically have distinctly different respiratory mechanics, and the biomechanical link between mechanical power and respiratory complications in patients in the operating room warrants further investigation. These patients typically show lower intrapleural pressures and increased tolerance to atelectasis and intrapulmonary shunting, which results in a lower vulnerability to mechanical ventilation considered harmful in critically ill patients. In addition, the loss of ventilated airspaces and the number of regional stressors may be smaller, allowing for mechanical ventilation with lower PEEP and driving pressure, thereby lowering the static (PEEP) and elastic dynamic (P_{plat} – PEEP) components of mechanical power.

We observed a considerable variability in mechanical power during intraoperative mechanical ventilation, which ranged from less than 4 J/min in patients in the lowest to up to 32 J/min in the highest quintile. Mechanical power in the second to fourth quintile still ranged between 4 and 10 J/min. Our broad patient cohort included a variety of patients, and a heterogeneity of pulmonary mechanics may explain this variability. In addition, we observed significant provider variability in the administration of mechanical power, even when adjusting for baseline patient and procedural characteristics, which may have further aggravated variability in the applied mechanical power during intraoperative ventilation.

The concept of mechanical power incorporates known key drivers of ventilator-induced lung injury, including tidal volume[23,36,37] and driving pressure.[23,38,39] Further studies reported an association between higher respiratory rates—another key component of mechanical power—and postoperative pulmonary complications in patients undergoing general anesthesia.[8] Ventilator settings often compete—for example, physicians increase the respiratory rate when decreasing tidal volume, as observed in previous randomized, controlled trials.[6] Results from studies showing no effect of lowering tidal volume may, therefore, be explained by the absence of a comprehensive focus on multiple factors that contribute to ventilator-induced lung injury[9] that can be provided through application of the mechanical power concept.

Our findings of an independent association of mechanical power after adjusting for driving pressure, respiratory rate, and tidal volume suggests that calculation of mechanical power adds information to the sum of these individual components. Our findings further corroborate a secondary analysis of three randomized, controlled trials in critically

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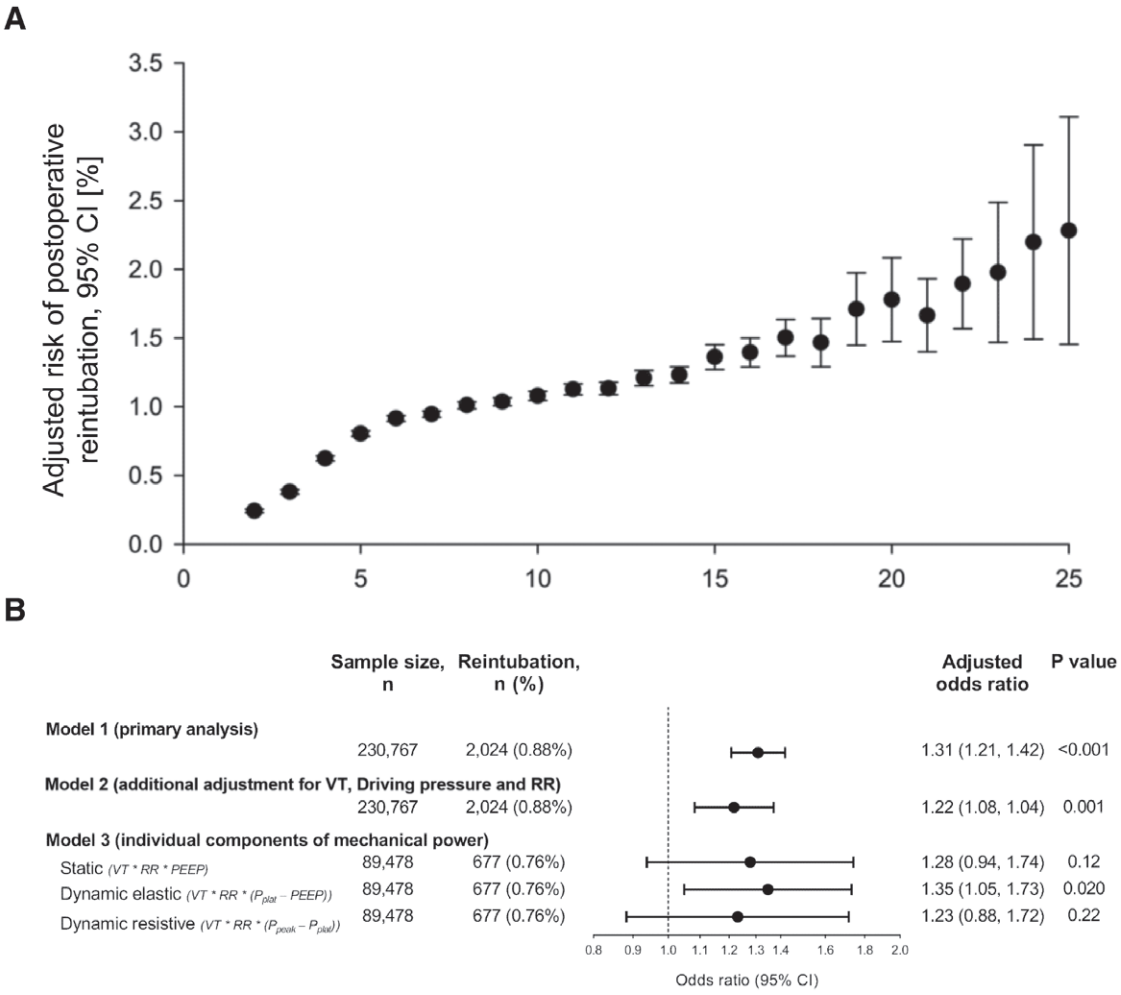


Fig. 4. Association of mechanical power and postoperative reintubation. (*A*) Adjusted risk of postoperative reintubation within 7 days by intraoperative mechanical power is shown. Marginal risk estimates were calculated based on the primary logistic regression model; estimates for reintubation are shown with 95% CI. Continuous mechanical power values were rounded to the nearest value. (*B*) Intraoperative mechanical power was significantly associated with greater odds of postoperative reintubation within 7 days in the primary analysis (model 1). When additionally adjusting the primary analysis for known drivers of ventilator-induced lung injury (model 2) including tidal volume (V_T), driving pressure, and respiratory rate (RR), the significant association remained robust. In model 3, we explored the individual association of the static, dynamic elastic, and dynamic resistive components of mechanical power with postoperative respiratory failure requiring reintubation by incorporating them as separate variables, instead of mechanical power, into the logistic regression model. Only the dynamic elastic component was associated with postoperative respiratory failure requiring reintubation, while the other two components showed no significant association with reintubation. PEEP, positive end-expiratory pressure; P_{peak}, peak pressure; P_{plat}, plateau pressure.

ill patients[40] and a limited *post hoc* analysis of a randomized, controlled trial in the operating room.[16] The lack of effectiveness in randomized controlled trials of intraoperative mechanical ventilation interventions may be explained by the absence of a comprehensive focus on the multiple factors that contribute to ventilator-induced lung injury[9]—for example, increasing respiratory rate might offset effects of decreasing tidal volume, as observed in previous studies.[6]

We found that only the dynamic elastic component was associated with greater risk of postoperative reintubation, but the static and dynamic resistive components were not. The isolation of this dynamic elastic element of mechanical power[15,41] reflects previous reports in patients with acute ARDS[19] and supports the need for further adjustment of the concept when estimating ventilator-induced lung injury,[42] for example by reducing noise from including the energy required to overcome airway resistance and elastic lung recoil.[15]

There are different options to modify mechanical power, which could be investigated in future, prospective

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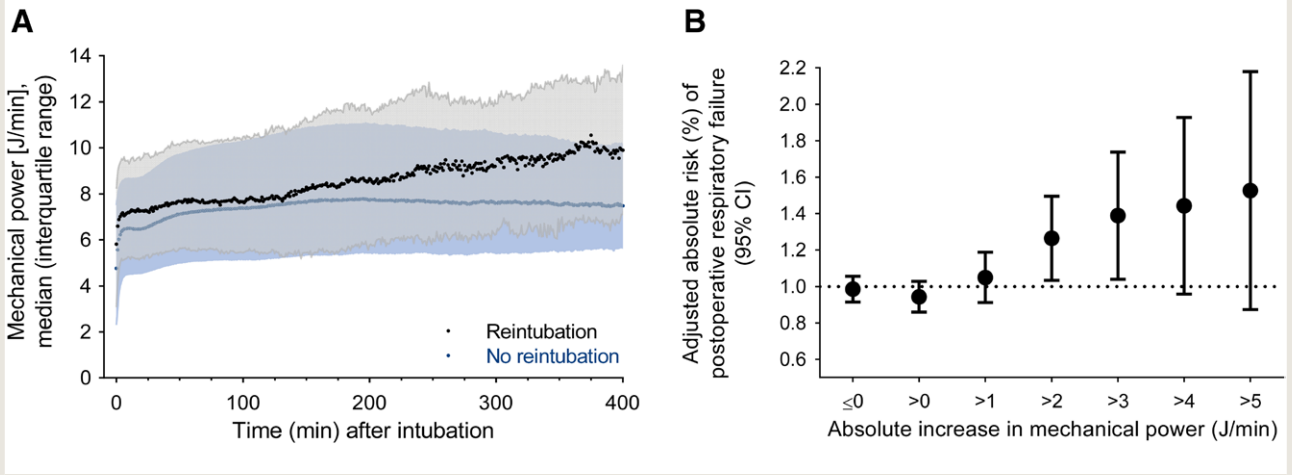


Fig. 5. Temporal trends in intraoperative mechanical power. (*A*) Changes in mechanical power over time during surgery are shown for patients with and without postoperative respiratory failure requiring reintubation. A significantly different temporal pattern in the intraoperative trend of mechanical power was observed between patients with and without postoperative respiratory failure ($P < 0.001$). In patients requiring postoperative reintubation, a constant linear increase in mechanical power was observed. (*B*) Adjusted absolute risk of postoperative respiratory failure requiring reintubation within 7 days for different thresholds of increases in mechanical power over time during surgery. Marginal risk estimates were calculated based on individual logistic regression models comparing cases with increases on mechanical power above each threshold to the reference group of cases with no increase in mechanical power (*i.e.*, less than or equal to 0 J/min); estimates for respiratory failure are shown with 95% CI.

studies. Based on the total work per unit time equation developed by Otis *et al.*,[43] tidal volume and respiratory rate can be optimized while maintaining a fixed minute ventilation (*i.e.*, through lowering one and increasing the other) to lower mechanical power.[44] Second, anesthesiologists may lower tidal volume and/or respiratory rate while allowing for permissive hypercapnia. These strategies might help to elucidate whether higher mechanical power and temporal changes in mechanical power are causal to ventilator-induced lung injury or an epiphenomenon of developing pulmonary failure.

The integration of competing parameters such as tidal volume and respiratory rate into a single value might aid clinicians when assessing mechanical ventilation and patients' pulmonary status while moving away from single ventilator parameters. Our results suggest that physicians should pay attention to patients that are ventilated with a high mechanical power, which may identify patients at risk of postoperative reintubation—an objective clinical outcome[8,20,22,23] and important hospital quality metric[45]—which is associated with greater mortality and hospitalization rates.[3] In an exploratory, *post hoc* defined analysis, we found that an intraoperative threshold increase of mechanical power by at least 2 J/min, which was driven by higher driving pressures and respiratory rates, was associated with 28% greater odds of developing postoperative respiratory failure. While these findings warrant confirmation in future studies, intraoperative assessment of mechanical power, which could be facilitated by real-time calculation based on computerized simulations, may assist in identification of patients at risk of developing postoperative respiratory failure.

Limitations

Due to the retrospective nature of our study, a cause–effect relationship between a higher mechanical power and postoperative respiratory failure cannot be determined. While we believe that our study provides important information of an association between these two variables based on real-world data, our data cannot show that modifying mechanical power will impact patient outcomes. Because of the low incidence (1%) of our primary outcome, it will be difficult to detect an effect of mechanical power modification on postoperative respiratory failure requiring reintubation in randomized, controlled trials.

We applied a simplified equation that allowed estimation of mechanical power in a large patient collective based on routinely recorded hospital registry data.[19] While this equation has been validated before[11] and was used in previous studies,[17,19] mechanical power is ideally calculated from continuous recordings of airway pressure and volume to achieve maximal granularity and accuracy.[15] The abbreviated formula might further lack accuracy when applied during pressure-controlled ventilation.[46] Furthermore, the clinical application of a concept originating from physics is inherently imperfect: power in physics is an eventual non-cumulative variable that does not increase in relation to the rate of fully repeatable events (*i.e.*, repetitive breathing

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cycles). Hence, the application of mechanical power might imply the load of delivered energy instead of pure physical power. The concept of mechanical power applied in our study[10,11] was derived to estimate the delivered energy during mechanical ventilation but not the retained or dissipated energy.[47] A more comprehensive approach would consider lungs as thermodynamic systems in which compartmental transfer of heat and work governs energy parameters, which could improve the accuracy of this concept when estimating ventilator-induced lung injury. However, this approach will be preserved for an experimental setting due to the impracticability of measuring heat transfer to patients' lungs. While our primary endpoint, postoperative reintubation, is an objective outcome that has been published before,[8,20,22,23] it may occur due to deteriorations other than respiratory failure. We addressed this by analyzing a more specific endpoint of postoperative pulmonary complications[35] in a subgroup of patients where these data were available, confirming our primary results.

Conclusions

Overall higher mechanical power identifies patients at risk of postoperative respiratory failure requiring reintubation in patients undergoing general anesthesia. Our findings suggest that this unifying concept adds information in addition to individual ventilator parameters and can facilitate identification of patients at risk of postoperative respiratory failure.

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Competing Interests

Dr. Houle has indicated financial relationships outside the submitted work with the American Society of Anesthesiologists (Schaumburg, Illinois) and the American Headache Society (Royal, New Jersey). Dr. Costa has received consulting fees from Timpel S.A. (São Paulo, Brazil), Magnamed S.A. (São Paulo, Brazil), and Getinge (Gothenburg, Sweden), outside the submitted work. Dr. Talmor received speaking fees and grant funds from Hamilton Medical, Inc. (Bonaduz, Switzerland), outside the submitted work. Dr. Baedorf-Kassis has received lecturing fees from Hamilton Medical, Inc., outside the submitted work and has received a KL2 award from Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health award No. KL2 TR002542). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health. Dr. Eikermann has received unrestricted funds from philanthropic donors Jeffrey and Judy Buzen during the conduct of the study, has received grants for investigator-initiated trials not related to this article from Merck & Co. (Kenilworth, New Jersey), and serves as a consultant on the advisory board of Merck & Co. Dr. Schaefer has received a grant for investigator-initiated trials not related to this article from Merck & Co. The other authors declare no competing interests.

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