Parameters for Simulation of Adult Subjects During Mechanical Ventilation

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BACKGROUND: Simulation studies are often used to examine ventilator performance. However, there are no standards for selecting simulation parameters. This study collected data in passively-ventilated adult human subjects and summarized the results as a set of parameters that can be used for simulation studies of intubated, passive, adult subjects with normal lungs, COPD, or ARDS. METHODS: Consecutive adult patients admitted to the ICU were included if they were deeply sedated and mechanically ventilated for <48 h without any spontaneous breathing activity. Subjects were classified as having normal lungs, COPD, or ARDS. Respiratory mechanics variables were collected once per subject. Static compliance was calculated as the ratio between tidal volume and driving pressure. Inspiratory resistance was measured by the least-squares fitting method. The expiratory time constant was estimated by the tidal volume/flow ratio. RESULTS: Of the 359 subjects included, 138 were classified as having normal lungs, 181 as ARDS, and 40 as COPD. Median (interquartile range) static compliance was significantly lower in ARDS subjects as compared with normal lung and COPD subjects (39 [32–50] mL/cm H_2O vs 54 [44–64] and 59 [43–75] mL/cm H_2O, respectively, $P < .001$). Inspiratory resistance was significantly higher in COPD subjects as compared with normal lung and ARDS subjects (22 [16–33] cm H_2O/L/s vs 13 [10–15] and 12 [9–14] cm H_2O/L/s, respectively, $P < .001$). The expiratory time constant was significantly different for each lung condition (0.60 [0.51–0.71], 1.07 [0.68–2.14], and 0.46 [0.40–0.55] s for normal lung, COPD, and ARDS subjects, respectively, $P < .001$). In the subgroup of subjects with ARDS, there were no significant differences in respiratory mechanics variables among mild, moderate, and severe ARDS. CONCLUSIONS: This study provides educators, researchers, and manufacturers with a standard set of practical parameters for simulating the respiratory system's mechanical properties in passive conditions. *Key words: medical simulation; critical care; artificial respiration; respiratory mechanics; ARDS; COPD; lung compliance; airway resistance*. [Respir Care 2018;63(2):158–168. © 2018 Daedalus Enterprises]

Introduction

Simulation studies are often used to examine ventilator performance because models of the respiratory system are much easier to understand and experiment with than real respiratory systems (either human or animal). According to the Society for Simulation in Healthcare, "Simulation is

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Dr Arnal has disclosed a relationship with Hamilton Medical AG. Mr Chatburn has disclosed relationships with CareFusion, Covidien, Dräger, Hamilton, IngMar Medical, Inogen, Invacare, Philips, ResMed, Neotech, and Breathe Technologies. The other authors have disclosed no conflicts of interest.

Mr Saoli presented a version of this work at the Congrès Réanimation, held January 11–13, 2017, in Paris, France.

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DOI: 10.4187/respcare.05775

the imitation or representation of one act or system by another. Healthcare simulations can be said to have four main purposes—education, assessment, research, and health system integration in facilitating patient safety."[1] Implicit in the concept of simulation is the understanding that the parameters of the simulation reflect realistic values of the system under study. If the model does not accurately represent the system being simulated, then any conclusions about the how the real system behaves are suspect.[1] More importantly, models can be created that do not vary with time or with ventilator settings, so that the differences observed in measurements are presumed to be related only to performance differences among the ventilators in the study.

In the past, studies reporting ventilator performance[2,3] often used some version of the Michigan Instruments Training and Test Lung simulator. This device has 1 or 2 spring-loaded bellows to model compliance (adjustable spring tension varies compliance values) connected in series with parabolic flow resistors. The Training and Test Lung is a passive device. To simulate inspiratory effort (muscle pressure [P_{mus}] in the equation of motion), researchers have improvised by linking the 2 bellows and using one to drive the other by connecting it to a separate ventilator.[4] Thus, the larger the tidal volume and the higher the inspiratory flow of the drive ventilator, the higher the simulated inspiratory effort. Unfortunately, this procedure limits the shape of the $P_{mus}(t)$ to the available flow shapes from the drive ventilator, which are quite limited. More recent studies[5-15] have used more sophisticated devices that allow high-fidelity simulation of both lung model (ie, resistance and compliance) and effort model (P_{mus} waveform).

As suggested above, studies simulating the mechanical properties of the respiratory system are common. Unfortunately, although international standards for ventilator performance testing (for manufacturers) are available (https://www.iso.org/standard/51141.html, *Accessed July 29, 2017*), there are no commonly accepted, clinically relevant standards for selecting simulation parameters that are evidence-based and linked to particular lung disease states (eg, normal, COPD, ARDS) or patient populations (eg, adult vs child vs infant). As a result, researchers typically pick values that seem reasonable to them, generally without regard to actual human data. This makes comparison of results among studies of ventilator performance difficult, and it makes meta-analysis impossible. Therefore, the purpose of this paper was to gather data on a large number of ventilated adult human subjects and to summarize the results as a set of parameters (grouped by lung disease) that can be used to construct standardized patients for simulation studies of intubated, passive patients (ie, all breaths are machine-triggered). In particular, we provide standardized values for respiratory system resistance and compliance that can be used in the equation of motion (either in physical or mathematical models). These values are grouped by lung condition: normal; COPD; and mild, moderate or severe ARDS.

QUICK LOOK

Current knowledge

Although international standards for ventilator performance testing are available, there are no commonly accepted, clinically relevant standards for selecting simulation parameters that are evidence-based and linked to particular lung disease states.

What this paper contributes to our knowledge

This study provides educators, researchers, and manufacturers with standardized values for respiratory system resistance and compliance that can be used in the equation of motion (either in physical or mathematical models) for simulating the respiratory system's mechanical properties according to lung condition: normal; COPD; and mild, moderate, or severe ARDS.

Methods

This prospective, observational, comparative study was conducted from June 2015 to November 2016 in the 16-bed general adult ICU of Sainte Musse Hospital in Toulon, France. The institutional review board approved the protocol, which was also declared at the Commission Nationale Informatique et Liberté. According to French regulation, signed consent was waived, and each patient's next of kin was informed by a document explaining the study and could refuse the patient's participation.

Subjects

Consecutive adult patients admitted in the ICU were included if they were deeply sedated (Richmond Agitation-Sedation Scale −4 or −5), were mechanically ventilated for <48 h without any spontaneous breathing activity, and met criteria for a single lung condition (normal lungs, COPD, or ARDS). Patients were excluded in case of pregnancy, body mass index >30 kg/m^2, severe hemodynamic impairment, bronchopleural fistula, brain death, or a mix of lung conditions (eg, COPD with ARDS). Sedation and myorelaxant were prescribed by the physician in charge of the subject, combining either midazolam or propofol with sufentanil, and cisatracurium were used. Subjects were positioned semirecumbently (30–45°) and mechanically ventilated using a Hamilton-S1 ventilator (Hamilton Medical, Rhäzüns, Switzerland).

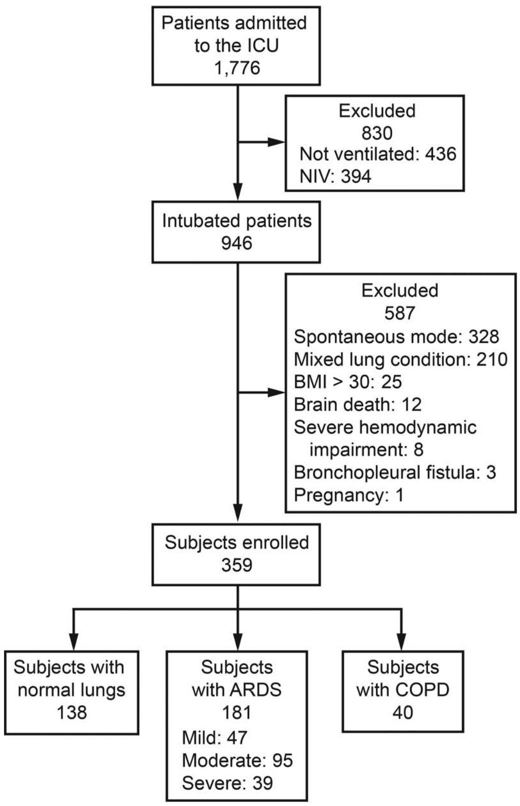

Fig. 1. Flow chart. NIV = noninvasive ventilation, BMI = body mass index.

A heat-and-moisture exchanger or a heated humidifier was used for gas conditioning.

Subjects were classified according to their lung condition as having normal lungs, COPD, or ARDS. Normal lungs was selected for subjects with no underlying respiratory disease, normal chest radiography on the inclusion day, and P_{aO_2}/F_{IO_2} ratio of ≥300 mm Hg; ARDS was defined according to the Berlin definition with an arterial blood gas measured at a minimum of 5 cm H_2O of PEEP;[16] COPD was defined using Global Initiative for Chronic Obstructive Lung Disease criteria.[17]

Ventilator Settings

All subjects were ventilated with the mode called INTELLiVENT-ASV.[18] Tidal volume (V_T) was automatically controlled to be in the range of 5–8 mL/kg predicted body weight for ARDS subjects, 6–9 mL/kg predicted body weight for normal lung subjects, and 7–10 mL/kg predicted body weight for COPD subjects. PEEP was automatically set in the range of 5–8 cm H_2O for normal lung subjects and 5–10 cm H_2O for COPD subjects, according to the PEEP-F_{IO_2} table implemented in INTELLiVENT-ASV, which is derived from the ARDSnet tables.[19] Plateau pressure was limited at 30 cm H_2O for all subjects.

Measurements, Data Collection, and Calculations

Airway pressure and flow were measured using the ventilator's proximal pneumotachograph (single-use flow sensor, PN 279331, Hamilton Medical, linear between −120 and 120 L/min with a ±5% error) inserted between the endotracheal tube and the Y-piece. When a heat-and-moisture exchanger was used, it was positioned distally to the sensor, so that measurements took into account the resistance of the heat-and-moisture exchanger. Volume was obtained by integration of the flow signal.

Table 1 Subject Characteristics at Inclusion

Characteristics	All Subjects	Normal Lungs	COPD	ARDS			
				All	Mild	Moderate	Severe
Number	359	138	40	181	47	95	39
Male/female sex, %	64/36	68/32	80/20	60/40	57/43	60/40	59/41
Age, median (IQR) y	67 (56–76)	65 (52–73)	66 (61–75)	68 (57–78)	68 (60–80)	69 (56–78)	67 (57–78)
BMI, median (IQR) kg/m^2	25 (22–28)	25 (22–27)	24 (22–27)	25 (22–29)	25 (22–28)	26 (22–29)	25 (22–29)
PBW, median (IQR) kg	66 (56–72)	66 (58–74)	66 (62–72)	63 (55–72)	63 (56–72)	64 (56–72)	62 (52–70)
SAPS II, median (IQR)	56 (46–68)	56 (47–67)	48 (41–64)	59 (49–71)	57 (50–66)	60 (48–73)	62 (48–74)
ETT size, median (IQR) mm	7.5 (7.5–8.0)	7.5 (7.5–8.0)	7.5 (7.5–8.0)	7.5 (7.5–8.0)	7.5 (7.5–8.0)	7.5 (7.5–8.0)	7.5 (7.5–8.0)
Humidification, %HH/%HME	74/26	53/47	82/18	88/12	81/19	86/14	100/0
Muscle relaxant, *n* (%)	132 (37)	26 (20)	11 (27)	95 (52)	12 (25)	55 (58)	28 (72)

IQR = interquartile range
BMI = body mass index
PBW = predicted body weight
ETT = endotracheal tube
HH = heated humidifier
HME = heat-and-moisture exchanger

Table 2 Ventilator Settings and Arterial Blood Gas Results

Settings	All Subjects (N = 359)	Normal Lungs (n = 138)	COPD (n = 40)	ARDS			
				All (n = 181)	Mild (n = 47)	Moderate (n = 95)	Severe (n = 39)
PEEP, cm H_2O	8 (5–12)	5 (5–7)	7 (5–10)	12 (9–15)	10 (7–12)	12 (9–15)	12 (10–16)
F_{IO_2}	0.3 (0.26–0.42)	0.26 (0.21–0.30)	0.32 (0.28–0.42)	0.38 (0.30–0.50)	0.31 (0.28–0.37)	0.40 (0.30–0.50)	0.48 (0.34–0.78)
V_T, mL/kg PBW	7.0 (6.2–8.0)	7.4 (6.4–8.2)	8.9 (7.3–10.9)	6.7 (5.7–7.4)	6.9 (6.3–7.5)	6.6 (5.6–7.2)	6.6 (5.6–7.5)
Frequency, breaths/min	19 (15–22)	17 (14–21)	14 (9–17)	21 (17–24)	20 (17–22)	21 (17–24)	21 (16–26)
P_{plat}, cm H_2O	19 (16–24)	15 (13–17)	20 (17–23)	23 (20–26)	21 (18–25)	23 (20–25)	25 (22–27)
pH	7.35 (7.28–7.41)	7.38 (7.33–7.43)	7.32 (7.26–7.40)	7.32 (7.26–7.40)	7.33 (7.28–7.40)	7.33 (7.26–7.41)	7.29 (7.21–7.34)
P_{aO_2}, mm Hg	83 (73–95)	89 (81–97)	78 (67–99)	80 (71–90)	81 (72–88)	78 (70–94)	78 (68–91)
P_{aCO_2}, mm Hg	40 (37–47)	37 (35–39)	51 (45–55)	43 (38–50)	39 (37–46)	43 (39–50)	49 (44–56)
S_{aO_2}, %	96 (94–98)	97 (96–98)	95 (93–98)	95 (93–97)	96 (94–97)	95 (94–97)	94 (92–95)

Results are median (interquartile range).
V_T = tidal volume
PBW = predicted body weight
P_{plat} = plateau pressure

Table 3 Respiratory Mechanics Results for All Subjects

Parameters	All Subjects (N = 359)	Normal Lungs (n = 138)	COPD (n = 40)	ARDS (n = 181)	P
C_{STAT}, mL/cm H_2O	47 (38–58)	54 (44–64)	59 (43–75)	39 (32–50)	<.001
R_{INS} LSF, cm H_2O/L/s	12 (10–16)	13 (10–15)	22 (16–33)	12 (9–14)	<.001
RC_{EXP}, s	0.5 (0.4–0.7)	0.6 (0.5–0.7)	1.1 (0.7–2.1)	0.5 (0.4–0.6)	<.001
R_{EXP}, cm H_2O/L/s	13 (11–15)	12 (10–14)	18 (14–36)	14 (11–16)	<.001

Results are median (interquartile range). P values are from analysis of variance.
C_{STAT} = static compliance
R_{INS} LSF = inspiratory resistances measured by least-square fit method
RC_{EXP} = expiratory time constant
R_{EXP} = expiratory resistance calculated from RC_{EXP} and C_{STAT}

Respiratory mechanics variables and ventilator settings were collected once per subject at the exact time of an arterial blood gas measurement. The time of data collection was chosen to be apart from nursing care and medical procedures.

Static compliance was calculated as the ratio between V_T and driving pressure. Driving pressure was calculated as the difference between plateau pressure and total PEEP measured by a 5-s end-inspiratory and end-expiratory occlusion, respectively.[20] Because subjects were ventilated in pressure control mode (with an exponential decay of inspiratory flow waveform), inspiratory resistance was measured by the least squares fitting method over the full respiratory cycle.[21] The expiratory time constant was estimated by the V_T/flow ratio at 75% of the expiratory V_T.[22]

Statistical Methods

To perform subgroup analysis, the study was planned to stop after the inclusion of at least 100 normal lung subjects, 30 ARDS subjects for each severity subgroup, and 40 COPD subjects. Values are expressed as medians (interquartile range). Kruskal-Wallis analysis of variance was used to compare values between each type of lung conditions. Statistical significance was assumed for $P \leq .05$. Statistical analysis was performed using SigmaStat software 3.5 (SPSS, Chicago, Illinois).

Results

Among the 359 subjects included, 138 subjects were classified as normal lungs, 181 as ARDS, and 40 as COPD. Subjects' flow diagram and characteristics at inclusion are presented in Figure 1 and Table 1, respectively. Ventilator settings and arterial blood gas results are presented in Table 2.

Respiratory mechanics results are presented in Table 3 and Figure 2. Static compliance was significantly lower in ARDS subjects, as compared with normal lung and COPD subjects (39 [32–50] mL/cm H_2O vs 54 [44–64] and 59 [43–75] mL/cm H_2O, respectively, $P < .001$). Inspiratory resistance was significantly higher in COPD subjects as compared with normal lung and ARDS subjects (22 [16–33] cm H_2O/L/s vs 13 [10–15] and 12 [9–14] cm

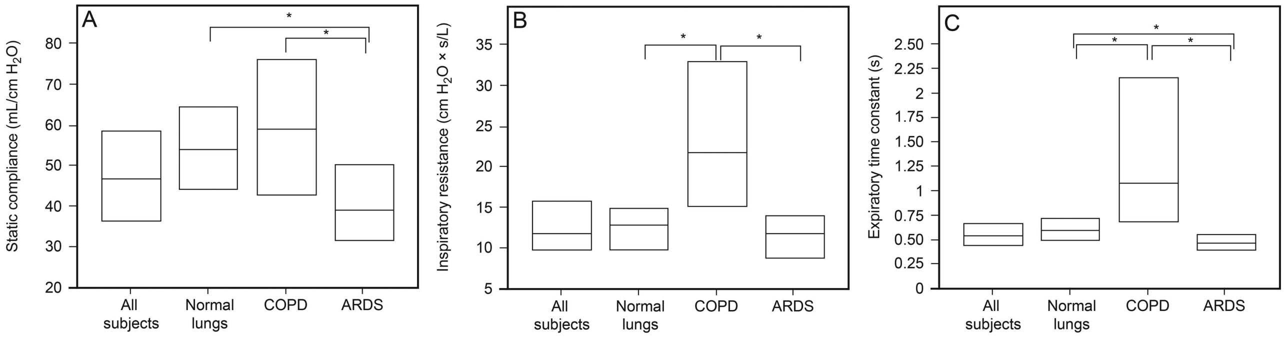

Fig. 2. Respiratory mechanics for all subjects and according to lung condition. Box plots represent median and interquartile range. * $P < .001$ for pairwise comparison using Dunn's method.

Table 4 Inspiratory Resistances According to Endotracheal Tube Size and Humidification

Parameters	All Subjects	Normal Lungs	COPD	ARDS	P
R_{INS} LSF with ETT 7.0, cm H_2O/L/s					
All	14 (13–16)	14 (13–15)	NA	15 (13–17)	
HH	14 (13–16)	13 (13–14)	NA	14 (13–16)	
HME	16 (13–19)	15 (13–18)	NA	17 (14–22)	
R_{INS} LSF with ETT 7.5, cm H_2O/L/s					
All	13 (11–16)	13 (11–15)	27 (18–39)	12 (10–14)	<.001
HH	12 (10–14)	11 (9–14)	33 (19–42)	11 (10–13)	<.001
HME	15 (12–16)	14 (12–16)	26 (16–29)	14 (12–17)	.02
R_{INS} LSF with ETT 8.0, cm H_2O/L/s					
All	11 (9–14)	11 (10–13)	18 (12–23)	10 (8–13)	<.001
HH	11 (9–14)	10 (10–12)	18 (13–24)	10 (8–12)	<.001
HME	13 (11–14)	13 (11–14)	16 (12–20)	14 (10–17)	.63

Results are median (interquartile range). P values are from analysis of variance on ranks.
R_{INS} LSF = inspiratory resistance measured by least-square fit method
ETT = endotracheal tube
NA = not applicable
HH = heated humidifier
HME = heat and moisture exchanger

H_2O/L/s, respectively, $P < .001$). Inspiratory resistance according to the size of endotracheal tube and humidification system are presented in Table 4. Expiratory time constant was significantly different for each lung condition (0.60 [0.51–0.71], 1.07 [0.68–2.14], and 0.46 [0.40–0.55] s for normal lung, COPD, and ARDS subjects, respectively, $P < .001$).

In the group of ARDS subjects, there were no significant differences in respiratory mechanics variables among mild, moderate, and severe ARDS subjects (Table 5 and Fig. 3).

Discussion

This study represents the largest single study describing respiratory system mechanical properties for all 3 populations commonly requiring mechanical ventilation in ICUs (ie, normal, COPD, and ARDS). As expected, all parameters show a large variation, yet median values permit distinction among patient populations and subpopulations (for ARDS) as shown in Tables 3 and 5. These median values are within the ranges of data reported in other studies for subjects with normal lungs,[23-33] subjects with COPD,[23-25,30,33,34] and subjects with ARDS (Tables 6–8).[23-28,30,35-61]

The question, of course, is what to do with all of this information. One obvious application, and the primary purpose of this study, is to provide the basis of simulation-based medical education and research, particularly in the art and science of mechanical ventilation.[62] Simulation-based medical education and simulation-based mastery learning have become well-established in undergraduate and graduate medical, nursing, and allied health-care training programs.[63] Much like a standardized patient,[64] a high-fidelity lung simulator can provide the framework for teaching virtually any aspect of the physical interaction of a patient and a mechanical ventilator. Furthermore, a stan-

Table 5 Respiratory Mechanics Results for the Subgroup of ARDS Subjects

Parameters	Mild ARDS (*n* = 47)	Moderate ARDS (*n* = 95)	Severe ARDS (*n* = 39)	*P*
C_{STAT}, mL/cm H_2O	44 (36–53)	39 (31–49)	38 (30–45)	.16
R_{INS} LSF, cm H_2O/L/s	11 (9–14)	12 (10–14)	12 (9–14)	.74
RC_{EXP}, s	0.50 (0.43–0.56)	0.44 (0.39–0.53)	0.45 (0.37–0.55)	.08
R_{EXP}, cm H_2O/L/s	13 (10–15)	14 (11–16)	14 (12–16)	.30

Results are median (interquartile range). *P* values are from analysis of variance.
C_{STAT} = static compliance
R_{INS} LSF = inspiratory resistance measured by least-square fit method
RC_{EXP} = expiratory time constant
R_{EXP} = expiratory resistances calculated from RC_{EXP} and C_{STAT}

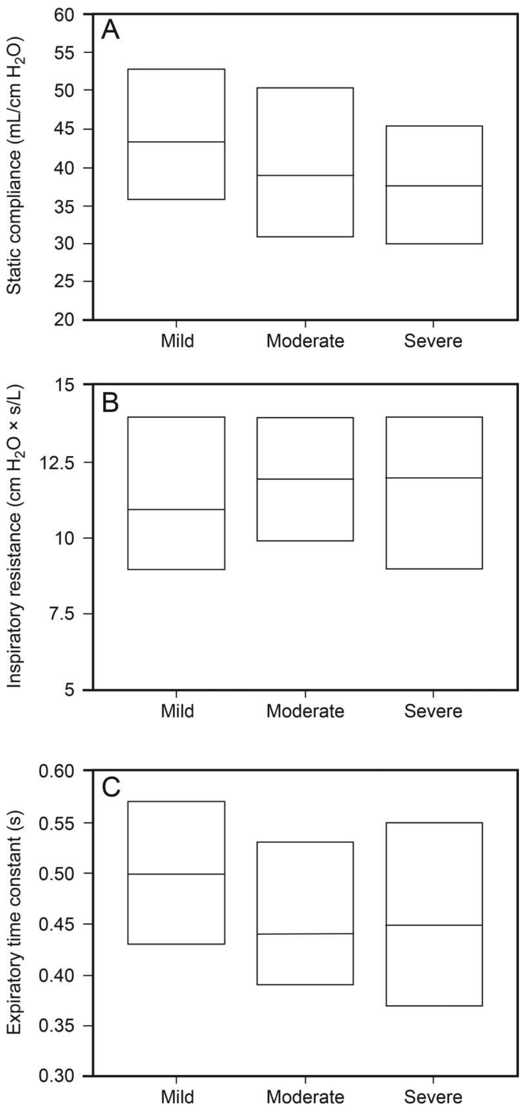

Fig. 3. Respiratory mechanics for ARDS subjects and according to severity: Box plots represent median and interquartile range.

dard set of simulation parameters would provide researchers with a common basis for conducting ventilator performance studies. Manufacturers of ventilators could also use this information for conducting realistic new product verification and validation studies.

Standard Simulation Parameters

A convenient theoretical basis for standardizing simulation parameters is a mathematical model of respiratory system mechanics. The simplest model of the respiratory system used for ventilator studies is the single-compartment model, composed of a single flow resistance and a single elastic compartment, represented by the equation of motion for the respiratory system,[65,66]

$$P_{vent}(t) + P_{mus}(t) - \text{auto-PEEP} = EV(t) + R\dot{V}(t) \quad (1)$$

where the following are true. P_{vent} (t) = the change in transrespiratory pressure difference (ie, airway opening pressure minus body surface pressure) as a function of time (t), measured relative to end-expiratory airway pressure. This is the pressure generated by a ventilator during an assisted breath. $P_{mus}(t)$ = ventilatory muscle pressure difference as a function of time (t); the theoretical chest wall transmural pressure difference that would produce movements identical to those produced by the ventilatory muscles during breathing maneuvers (positive during inspiratory effort, negative during expiratory effort). V(t) = volume change relative to end-expiratory volume as a function of time (t). $\dot{V}(t)$ = flow as a function of time (t), the first derivative of volume with respect to time. E = elastance (inverse of compliance; E = 1/C). R = resistance. auto-PEEP = end-expiratory alveolar pressure above end-expiratory airway pressure.

In this equation, pressure, volume, and flow are variables, whereas elastance and resistance are parameters (assumed to be constants). This happens to be the same model used by ventilators that calculate and display resistance and compliance values of patients. Indeed, the graphic waveforms for pressure, volume, and flow displayed by such ventilators are nothing other than the graphical representation of the equation of motion. The compliance (C) of the model is generally

Table 6 Respiratory Mechanics Results From Other Studies for Normal Subjects

Study	Year	Subjects, *N*	Method	C*	R_{INS}†	RC_{EXP}‡	R_{EXP}§	Definition of Normal
Arnal[23]	2008	115	LSF/75% expiration	40	16	0.78	20	Yes
Arnal[24]	2013	27	LSF/75% expiration	39	15	0.58	15	No
Arnal (unpublished)	2015	20	LSF/75% expiration	51	14	0.65	13	No
Belliato[25]	2004	8	LSF/75% expiration	49	12	0.72	15	No
Chang[26]	2013	722	Conventional	39	NR	NR	NR	No
Chiumello[27]	2008	19	Conventional	56	NR	NR	NR	No
Fretschner[28]	1996	10	LSF/75% expiration	56	NR	NR	NR	No
Futier[29]	2013	400	Conventional	53	NR	NR	NR	No
Iotti[30]	2010	22	LSF/75% expiration	51	13	0.71	14	No
Jia[31]	2008	636	Conventional	46	NR	NR	NR	No
Koutsoukou[32]	2006	21	Conventional	NR	10	NR	NR	No
Volta[33]	2002	8	Conventional	NR	12	NR	NR	No

* Median = 50; maximum = 56; minimum = 39.
† Median = 13; maximum = 16; minimum = 10.
‡ Median = 0.7; maximum = 0.8; minimum = 0.6.
§ Median = 15; maximum = 20; minimum = 13.
C = compliance
R_{INS} = inspiratory resistance
RC_{EXP} = expiratory time constant
R_{EXP} = expiratory resistance calculated from RC_{EXP} and C
LSF = least-square fit method
NR = not reported

Table 7 Respiratory Mechanics Results From Other Studies for Subjects With COPD

Study	Year	Subjects, *N*	Method	C*	R_{INS}†	RC_{EXP}‡	R_{EXP}§	Definition of COPD
Arnal[23]	2008	33	LSF/75% expiration	48	21	1.00	21	GOLD
Arnal[24]	2013	12	LSF/75% expiration	53	21	1.22	23	GOLD
Arnal (unpublished)	2015	9	LSF/75% expiration	58	23	1.13	19	GOLD
Belliato[25]	2004	8	LSF/75% expiration	65	25	2.21	34	ATS
Iotti[30]	2010	30	LSF/75% expiration	55	20	1.08	20	No
Lourens[34]	2000	8	75% expiration	NR	NR	1.05	NR	Moderate COPD
Lourens[34]	2000	18	75% expiration	NR	NR	2.84	NR	Severe COPD
Volta[33]	2002	8	Conventional	NR	20	NR	NR	No

* Median = 55; maximum = 65; minimum = 48.
† Median = 21; maximum = 25; minimum = 20.
‡ Median = 1.1; maximum = 2.8; minimum = 1.0.
§ Median = 21; maximum = 34; minimum = 19.
C = compliance
R_{INS} = inspiratory resistance
RC_{EXP} = expiratory time constant
R_{EXP} = expiratory resistance calculated from RC_{EXP} and C
LSF = least-square fit method
GOLD = Global Initiative for Chronic Obstructive Lung Disease
ATS = American Thoracic Society
NR = not reported

assumed to be linear for ventilator performance studies, in the form of C = Δvolume/Δpressure. The resistance (R) is modeled as either linear (R = Δpressure/Δflow) or non-linear (eg, parabolic). A parabolic resistor is one for which pressure is proportional to the square of flow. Note that for a parabolic resistor, the resistance is often defined as Δpressure/Δflow at a particular flow value. This means that the equivalent linear resistance is different for each flow at which it is evaluated. In other words, using a parabolic resistor, the resistive load of the lung model changes as flow changes. Hence, to maintain consistent testing parameters across different flows, it is usually better to select linear rather than parabolic resistors for ventilator performance evaluation studies.

To our knowledge, this study is the first attempt to provide standardized, evidence-based simulation parameters for the mechanical properties of the adult human re-

Table 8 Respiratory Mechanics Results From Other Studies for Subjects With ARDS

First Author	Year	Subjects, *N*	Method	C*	R_{INS}†	RC_{EXP}‡	R_{EXP}§	Definition of ARDS
Amato[35]	1998	53	Conventional	29	NR	NR	NR	
Brower[36]	2004	474	Conventional	35	NR	NR	NR	AECC
Arnal[23]	2008	26	LSF/75% expiration	27	15	0.51	19	AECC
Arnal[24]	2013	13	LSF/75% expiration	29	11	0.47	16	AECC
Arnal[37]	2011	50	LSF/75% expiration	30	NR	NR	NR	AECC
Arnal[38]	2012	31	LSF/75% expiration	35	16	NR	NR	AECC
Belliato[25]	2004	5	LSF/75% expiration	26	13	0.47	18	AECC
Brower[39]	2003	96	Conventional	35	NR	NR	NR	AECC
Caironi[40]	2010	68	Conventional	43	NR	NR	NR	AECC
Chang[26]	2013	107	Conventional	32	NR	NR	NR	AECC
Chiumello[27]	2008	24	Conventional	42	NR	NR	NR	AECC
Chiumello[41]	2013	51	Conventional	37	NR	NR	NR	AECC
Chiumello[42]	2013	44	Conventional	42	NR	NR	NR	Berlin
Cressoni[43]	2014	148	Conventional	43	NR	NR	NR	Berlin
Dellamonica[44]	2011	30	Conventional	31	NR	NR	NR	AECC
Dellamonica[45]	2013	40	Conventional	36	NR	NR	NR	AECC
Demory[46]	2008	26	LSF/75% expiration	32	NR	NR	NR	AECC
Estenssoro[47]	2003	48	Conventional	26	NR	NR	NR	AECC
Galiatsou[48]	2006	21	Conventional	30	NR	NR	NR	AECC
Gattinoni[49]	2006	68	Conventional	44	NR	NR	NR	AECC
Iotti[30]	2010	36	LSF/75% expiration	34	15	0.5	15	AECC
Mercat[50]	2008	767	Conventional	36	NR	NR	NR	AECC
Morán[51]	2011	13	Conventional	28	NR	NR	NR	AECC
Nuckton[52]	2002	179	Conventional	30	NR	NR	NR	AECC
Oczenski[53]	2004	30	Conventional	35	NR	NR	NR	AECC
Osman[54]	2009	145	Conventional	32	NR	NR	NR	AECC
Papazian[55]	2010	339	Conventional	31	NR	NR	NR	AECC
Talmor[56]	2008	61	Conventional	36	NR	NR	NR	AECC
Terragni[57]	2007	30	Conventional	26	NR	NR	NR	AECC
Thille[58]	2007	71	Conventional	35	NR	NR	NR	AECC
Villagrá[59]	2002	17	Conventional	33	NR	NR	NR	AECC
Villar[60]	2007	170	Conventional	32	NR	NR	NR	AECC
Wallet[61]	2013	14	Conventional	44	NR	NR	NR	AECC

* Median = 33; maximum = 44; minimum = 26.
† Median = 15; maximum = 16; minimum = 11.
‡ Median = 0.5; maximum = 0.5; minimum = 0.5.
§ Median = 17; maximum = 19; minimum = 15.
C = compliance
R_{INS} = inspiratory resistance
RC_{EXP} = expiratory time constant
R_{EXP} = expiratory resistance calculated from RC_{EXP} and C
LSF = least-square fit method
AECC = American-European consensus conference
NR = not reported

spiratory system linked to realistic, general mechanical ventilator settings and patient demographics. In creating our recommendations, we necessarily must summarize and simplify the data at hand. Hence, we have condensed the information from the previous tables in Table 9. We have also simplified it by rounding values to whole numbers for convenience while maintaining the general magnitude of the parameter within realistic ranges, as indicated by our study and those of others. Obviously, we could have selected other values, but these seem to be reasonable, within the specifications of available mechanical simulators, and perhaps also fairly easily manufactured from scratch (eg, rubber test lungs with variable resistance and compliance settings or rigid walled lung models).[67]

Our study is limited by the fact that it was conducted at a single institution with a single mode of ventilation. To the extent that a mode of ventilation and a particular style of clinical management (including selection of optimum PEEP levels) can influence the mechanical properties of various populations of patients, our data are biased. How-

Table 9 Standardized Parameters for Simulation of Mechanical Ventilation in the Adult

Parameters	Normal	COPD	ARDS			
			All	Mild	Moderate	Severe
C_{STAT}, mL/cm H_2O	50	60	40	45	40	35
HH − R_{INS}, cm H_2O/L/s	10	20	10	10	10	10
HH − RC, s	0.50	1.20	0.35	0.45	0.35	0.25
HME − R_{INS}, cm H_2O/L/s	15	25	15	15	15	15
HME − RC, s	0.75	1.50	0.53	0.68	0.53	0.38

C_{STAT} = static compliance
HH = heated humidifier
R_{INS} = inspiratory resistance
HME = heat-and-moisture exchanger
RC = time constant

ever, the bias may be trivial, given the favorable comparison of our median values with those of a vast number of previous studies. Furthermore, our data are not intended to be optimal or even benchmark values for actual patient care. Another limitation is that all measurements were performed in passively ventilated subjects. Respiratory mechanics variables (ie, resistance and compliance) are the same in passively and actively breathing patients during assisted ventilation, other factors being essentially equal (eg, V_T and flow). The main problem with simulation of the spontaneously breathing patient is the effort model parameters (ie, P_{mus} waveform characteristics).

Conclusions

Effort model parameters are difficult to evaluate during mechanical ventilation with the current technology, and they have a lot of variability. However, having reasonable values for passive mechanics (such as the results of our study), future researchers may then impose any effort model parameters they can imagine for the intended simulation study. In conclusion, this study provides educators, researchers, and manufacturers with a standard set of practical, evidence-based parameters for simulating the respiratory system's mechanical properties under passive conditions.

REFERENCES

1. Chatburn RL. Simulation studies for device evaluation. Respir Care 2014;59(4):e61-e66.
2. Blakeman TC, Branson RD. Evaluation of 4 new generation portable ventilators. Respir Care 2013;58(2):264-272.
3. Wallon G, Bonnet A, Guérin C. Delivery of tidal volume from four anaesthesia ventilators during volume-controlled ventilation: a bench study. Br J Anaesth 2013;110(6):1045-1051.
4. Blakeman TC, Rodriquez D Jr, Hanseman D, Branson RD. Bench evaluation of 7 home-care ventilators. Respir Care 2011;56(11):1791-1798.
5. Garnier M, Quesnel C, Fulgencio JP, Degrain M, Carteaux G, Bonnet F, et al. Multifaceted bench comparative evaluation of latest intensive care unit ventilators. Br J Anaesth 2015;115(1):89-98.
6. Chatburn RL, Mireles-Cabodevila E, Sasidhar M. Tidal volume measurement error in pressure control modes of mechanical ventilation: A model study. Comput Biol Med 2016;75:235-242.
7. Vasconcelos RS, Sales RP, Melo LHP, Marinho LS, Bastos VP, Nogueira ADN, et al. Influences of duration of inspiratory effort, respiratory mechanics, and ventilator type on asynchrony with pressure support and proportional assist ventilation. Respir Care 2017; 62(5):550-557.
8. Itagaki T, Chenelle CT, Bennett DJ, Fisher DF, Kacmarek RM. Effects of leak compensation on patient-ventilator synchrony during premature/neonatal invasive and noninvasive ventilation: a lung model study. Respir Care 2017;62(1):22-33.
9. Itagaki T, Bennett DJ, Chenelle CT, Fisher DF, Kacmarek RM. Performance of leak compensation in all-age ICU ventilators during volume-targeted neonatal ventilation: a lung model study. Respir Care 2017;62(1):10-21.
10. Vasconcelos Rdos S, Melo LH, Sales RP, Marinho LS, Deulefeu FC, Reis RC, et al. Effect of an automatic triggering and cycling system on comfort and patient-ventilator synchrony during pressure support ventilation. Respiration 2013;86(6):497-503.
11. Volsko TA, Hoffman J, Conger A, Chatburn RL. The effect of targeting scheme on tidal volume delivery during volume control mechanical ventilation. Respir Care 2012;57(8):1297-1304.
12. Mireles-Cabodevila E, Chatburn RL. Work of breathing in adaptive pressure control continuous mandatory ventilation. Respir Care 2009; 54(11):1467-1472.
13. Terado M, Ichiba S, Nagano O, Ujike Y. Evaluation of pressure support ventilation with seven different ventilators using Active Servo Lung 5000. Acta Med Okayama 2008;62(2):127-133.
14. Chen Y, Cheng K, Zhou X. Performance characteristics of seven bilevel mechanical ventilators in pressure-support mode with different cycling criteria: a comparative bench study. Med Sci Monit 2015;21:310-317.
15. Chen Y, Cheng K, Zhou X. Effectiveness of inspiratory termination synchrony with automatic cycling during noninvasive pressure support ventilation. Med Sci Monit 2016;22:1694-1701.
16. Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med 2012; 38(10):1573-1582.
17. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187(4):347-365.
18. Chatburn RL, El-Khatib M, Mireles-Cabodevila E. A taxonomy for mechanical ventilation: 10 fundamental maxims. Respir Care 2014; 59(11):1747-1763.
19. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.
20. Lucangelo U, Bernabè F, Blanch L. Lung mechanics at the bedside: make it simple. Curr Opin Crit Care 2007;13(1):64-72.
21. Iotti GA, Braschi A, Brunner JX, Smits T, Olivei M, Palo A, Veronesi R. Respiratory mechanics by least squares fitting in mechanically ventilated patients: applications during paralysis and during pressure support ventilation. Intensive Care Med 1995;21(5):406-413.
22. Brunner JX, Laubscher TP, Banner MJ, Iotti G, Braschi A. Simple method to measure total expiratory time constant based on the pas-

sive expiratory flow-volume curve. Crit Care Med 1995;23(6):1117-1122.
23. Arnal JM, Wysocki M, Nafati C, Donati S, Granier I, Corno G, Durand-Gasselin J. Automatic selection of breathing pattern using adaptive support ventilation. Intensive Care Med 2008;34(1):75-81.
24. Arnal JM, Garnero A, Novonti D, Demory D, Ducros L, Berric A, et al. Feasibility study on full closed-loop control ventilation (IntelliVent-ASV) in ICU patients with acute respiratory failure: a prospective observational comparative study. Crit Care 2013;17(5):R196.
25. Belliato M, Palo A, Pasero D, Iotti GA, Mojoli F, Braschi A. Evaluation of adaptive support ventilation in paralysed patients and in a physical lung model. Int J Artif Organs 2004;27(8):709-716.
26. Chang SY, Dabbagh O, Gajic O, Patrawalla A, Elie MC, Talmor DS, et al. Contemporary ventilator management in patients with and at risk of ALI/ARDS. Respir Care 2013;58(4):578-588.
27. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 2008;178(4):346-355.
28. Fretschner R, Laubscher TP, Brunner JX. New aspects of pulmonary mechanics: "slowly" distensible compartments of the respiratory system, identified by a PEEP step maneuver. Intensive Care Med 1996; 22(12):1328-1334.
29. Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013;369(5):428-437.
30. Iotti GA, Polito A, Belliato M, Pasero D, Beduneau G, Wysocki M, et al. Adaptive support ventilation versus conventional ventilation for total ventilatory support in acute respiratory failure. Intensive Care Med 2010;36(8):1371-1379.
31. Jia X, Malhotra A, Saeed M, Mark RG, Talmor D. Risk factors for ARDS in patients receiving mechanical ventilation for >48 h. Chest 2008;133(4):853-861.
32. Koutsoukou A, Perraki H, Raftopoulou A, Koulouris N, Sotiropoulou C, Kotanidou A, et al. Respiratory mechanics in brain-damaged patients. Intensive Care Med 2006;32(12):1947-1954.
33. Volta CA, Marangoni E, Alvisi V, Capuzzo M, Ragazzi R, Pavanelli L, Alvisi R. Respiratory mechanics by least squares fitting in mechanically ventilated patients: application on flow-limited COPD patients. Intensive Care Med 2002;28(1):48-52.
34. Lourens MS, van den Berg B, Aerts JG, Verbraak AF, Hoogsteden HC, Bogaard JM. Expiratory time constants in mechanically ventilated patients with and without COPD. Intensive Care Med 2000; 26(11):1612-1618.
35. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998;338(6):347-354.
36. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 2004;351(4):327-336.
37. Arnal JM, Paquet J, Wysocki M, Demory D, Donati S, Granier I, et al. Optimal duration of a sustained inflation recruitment maneuver in ARDS patients. Intensive Care Med 2011;37(10):1588-1594.
38. Arnal JM, Wysocki M, Novotni D, Demory D, Lopez R, Donati S, et al. Safety and efficacy of a fully closed-loop control ventilation (IntelliVent-ASV(R)) in sedated ICU patients with acute respiratory failure: a prospective randomized crossover study. Intensive Care Med 2012;38(5):781-787.
39. Brower RG, Morris A, MacIntyre N, Matthay MA, Hayden D, Thompson T, et al. Effects of recruitment maneuvers in patients with acute lung injury and acute respiratory distress syndrome ventilated with high positive end-expiratory pressure. Crit Care Med 2003;31(11): 2592-2597.
40. Caironi P, Cressoni M, Chiumello D, Ranieri M, Quintel M, Russo SG, et al. Lung opening and closing during ventilation of acute respiratory distress syndrome. Am J Respir Crit Care Med 2010; 181(6):578-586.
41. Chiumello D, Marino A, Cressoni M, Mietto C, Berto V, Gallazzi E, et al. Pleural effusion in patients with acute lung injury: a CT scan study. Crit Care Med 2013;41(4):935-944.
42. Chiumello D, Coppola S, Froio S, Mietto C, Brazzi L, Carlesso E, Gattinoni L. Time to reach a new steady state after changes of positive end expiratory pressure. Intensive Care Med 2013;39(8): 1377-1385.
43. Cressoni M, Cadringher P, Chiurazzi C, Amini M, Gallazzi E, Marino A, et al. Lung inhomogeneity in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2014;189(2):149-158.
44. Dellamonica J, Lerolle N, Sargentini C, Beduneau G, Di Marco F, Mercat A, et al. PEEP-induced changes in lung volume in acute respiratory distress syndrome: two methods to estimate alveolar recruitment. Intensive Care Med 2011;37(10):1595-1604.
45. Dellamonica J, Lerolle N, Sargentini C, Hubert S, Beduneau G, Di Marco F, et al. Effect of different seated positions on lung volume and oxygenation in acute respiratory distress syndrome. Intensive Care Med 2013;39(6):1121-1127.
46. Demory D, Arnal JM, Wysocki M, Donati S, Granier I, Corno G, Durand-Gasselin J. Recruitability of the lung estimated by the pressure volume curve hysteresis in ARDS patients. Intensive Care Med 2008;34(11):2019-2025.
47. Estenssoro E, Dubin A, Laffaire E, Canales HS, Sáenz G, Moseinco M, Bachetti P. Impact of positive end-expiratory pressure on the definition of acute respiratory distress syndrome. Intensive Care Med 2003;29(11):1936-1942.
48. Galiatsou E, Kostanti E, Svarna E, Kitsakos A, Koulouras V, Efremidis SC, Nakos G. Prone position augments recruitment and prevents alveolar overinflation in acute lung injury. Am J Respir Crit Care Med 2006;174(2):187-197.
49. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med 2006;354(17):1775-1786.
50. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2008;299(6):646-655.
51. Morán I, Blanch L, Fernández R, Fernández-Mondéjar E, Zavala E, Mancebo J. Acute physiologic effects of a stepwise recruitment maneuver in acute respiratory distress syndrome. Minerva Anestesiol 2011;77(12):1167-1175.
52. Nuckton TJ, Alonso JA, Kallet RH, Daniel BM, Pittet JF, Eisner MD, Matthay MA. Pulmonary dead-space fraction as a risk factor for death in the acute respiratory distress syndrome. N Engl J Med 2002;346(17):1281-1286.
53. Oczenski W, Hörmann C, Keller C, Lorenzl N, Kepka A, Schwarz S, Fitzgerald RD. Recruitment maneuvers after a positive end-expiratory pressure trial do not induce sustained effects in early adult respiratory distress syndrome. Anesthesiology 2004;101(3):620-625.
54. Osman D, Monnet X, Castelain V, Anguel N, Warszawski J, Teboul JL, et al. Incidence and prognostic value of right ventricular failure in acute respiratory distress syndrome. Intensive Care Med 2009; 35(1):69-76.
55. Papazian L, Forel JM, Gacouin A, Penot-Ragon C, Perrin G, Loundou A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010;363(12):1107-1116.

56. Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359(20):2095-2104.
57. Terragni PP, Rosboch G, Tealdi A, Corno E, Menaldo E, Davini O, et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 2007;175(2):160-166.
58. Thille AW, Richard JC, Maggiore SM, Ranieri VM, Brochard L. Alveolar recruitment in pulmonary and extrapulmonary acute respiratory distress syndrome: comparison using pressure-volume curve or static compliance. Anesthesiology 2007;106(2):212-217.
59. Villagrá A, Ochagavía A, Vatua S, Murias G, Del Mar Fernández M, Lopez Aguilar J, et al. Recruitment maneuvers during lung protective ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 2002;165(2):165-170.
60. Villar J, Pérez-Méndez L, López J, Belda J, Blanco J, Saralegui I, et al. An early PEEP/F_{IO_2} trial identifies different degrees of lung injury in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2007;176(8):795-804.
61. Wallet F, Delannoy B, Haquin A, Debord S, Leray V, Bourdin G, et al. Evaluation of recruited lung volume at inspiratory plateau pressure with PEEP using bedside digital chest X-ray in patients with acute lung injury/ARDS. Respir Care 2013;58(3):416-423.
62. Yee J, Fuenning C, George R, Hejal R, Haines N, Dunn D, et al. Mechanical ventilation boot camp: a simulation-based pilot study. Crit Care Res Pract 2016;2016:4670672.
63. Okla G, Eden D, Okla N. Simulation lab: "a contemporary medical essential". Middle East J Anaesthesiol 2016;23(4):501-503.
64. Adamo G. Simulated and standardized patients in OSCEs: achievements and challenges 1992-2003. Med Teach 2003;25(3):262-270.
65. Henderson WR, Chen L, Amato MB, Brochard LJ. Fifty years of research in ARDS: respiratory mechanics in acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;196(7):822-833.
66. Primiano FP Jr., Chatburn RL. Zen and the art of nomenclature maintenance: a revised approach to respiratory symbols and terminology. Respir Care 2006;51(12):1458-1470.
67. Hill DW, Moore V. The action of adiabatic effects on the compliance of an artificial thorax. Br J Anaesth 1965;37:19-22.