

Prone Position Improves Lung Mechanical Behavior and Enhances Gas Exchange Efficiency in Mechanically Ventilated Chronic Obstructive Pulmonary Disease Patients

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Pronation might favorably affect respiratory system (rs) mechanics and function in volume-controlled, mode-ventilated chronic obstructive pulmonary disease (COPD) patients. We studied 10 COPD patients, initially positioned supine (baseline supine [$\text{supine}_{\text{BAS}}$]) and then randomly and consecutively changed to protocol supine ($\text{supine}_{\text{PROT}}$), semirecumbent, and prone positions. Rs mechanics and inspiratory work (W_I) were assessed at baseline (0.6 L) (all postures) and sigh (1.2 L) ($\text{supine}_{\text{BAS}}$ excluded) tidal volume (V_T) with rapid airway occlusion during constant-flow inflation. Hemodynamics and gas exchange were assessed in all postures. There were no complications. Prone positioning resulted in (a) increased dynamic-static chest wall (cw) elastance (at both V_T s) and improved oxygenation versus $\text{supine}_{\text{BAS}}$, $\text{supine}_{\text{PROT}}$, and semirecumbent, (b) decreased additional lung (L) resistance-elastance versus $\text{supine}_{\text{PROT}}$ and

semirecumbent at sigh V_T , (c) decreased L-static elastance (at both V_T s) and improved CO_2 elimination versus $\text{supine}_{\text{BAS}}$ and $\text{supine}_{\text{PROT}}$, and (d) improved oxygenation versus all other postures. Semirecumbent positioning increased mainly additional cw-resistance versus $\text{supine}_{\text{BAS}}$ and $\text{supine}_{\text{PROT}}$ at baseline. V_T W_I -subcomponent changes were consistent with changes in rs, cw, and L mechanical properties. Total rs- W_I and hemodynamics were unaffected by posture change. After pronation, five patients were repositioned supine ($\text{supine}_{\text{POSTPRO}}$). In $\text{supine}_{\text{POSTPRO}}$, static rs-L elastance were lower, and oxygenation was still improved versus $\text{supine}_{\text{BAS}}$. Pronation of mechanically ventilated COPD patients exhibits applicability and effectiveness and improves oxygenation and sigh-L mechanics versus semirecumbent ("gold standard") positioning.

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Depending on respiratory system (rs) pathology, body posture differentially affects chest wall (cw), lung (L) mechanics, and gas exchange during artificial respiration (1,2). In chronic obstructive pulmonary disease (COPD), posture change rs-effects are still unclear. Severe COPD is often associated with cor pulmonale, potentially causing L-compression and L-elastance increase, especially in the supine position. We theorized that in mechanically ventilated COPD patients, prone positioning may reduce L-elastance, increase cw-elastance, and improve gas exchange efficiency relative to supine and semirecumbent ("gold standard") positioning.

Methods

IRB approval, nonwritten patient consent (whenever feasible), and informed written next-of-kin consent (always) were obtained (1,3). We studied 10 moderate-to-severe COPD patients (4) (Table 1), orotracheally intubated (8.0–8.5 mm internal diameter [ID], 26-cm long endotracheal tube [ETT], Portex, UK) mechanically ventilated (Siemens 300C, Germany) because of acute respiratory failure (ARF) (PaO_2 -inspired O_2 fraction [FIO_2], 75–184 mm Hg; PaCO_2 , 61.0–101.4 mm Hg) secondary to severe, acute bronchitis (5).

Exclusion criteria were left ventricular failure, acute myocardial ischemia, L-lobe atelectasis, pneumonia, sepsis, pulmonary embolism, and mean pulmonary artery pressure (MPAP) ≥ 30 mm Hg. During the 4.5- to 5-h study period, patient care was provided by a physician uninvolved in the study. Any new or additional administration of IV fluid boluses,

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Table 1. Individual Patient Characteristics Before and After Hospital Admission and Initial Inhospital Management

Patent no.	Age (yr)	Sex	Body mass index (kg/m ²)	Smoking (pack-yr) ^a	Predominant component of COPD ^b	Comorbidity	Evolution of COPD (yr)	No. of exacerbations within preceding 12 mo
1	59	Male	24.2	46	Pulmonary emphysema	HT	9	1
2	69	Female	22.4	102	Chronic bronchitis	HT, AF ^c , CVD	16	1
3	58	Male	23.5	105	Chronic bronchitis	None	7	2
4	71	Male	27.5	81	Chronic bronchitis	HT, CAD, MD	13	1
5	67	Male	32.3	69	Chronic bronchitis	HT, DM, OB, CAD	26	5
6	74	Female	22.5	50	Chronic bronchitis	HT, MAT ^e PVD, MD ^d	17	2
7	56	Male	24.4	80	Chronic bronchitis	None	8	3
8	61	Male	19.2	115	Pulmonary emphysema	HT	10	4
9	63	Female	27.2	86	Chronic bronchitis	HT	14	2
10	72	Male	27.1	80	Chronic bronchitis	HT, DM, CAD, PVD, CVD	23	2

Patient no.	FEV1 (% of predicted) ^b	FVC (% of predicted) ^b	FEV1/FVC (% of predicted) ^b	Admitted to the ICU from hospital ward/emergency room, before/after ETI	APACHE II score just before ETI	Initial ICU airway/ventilatory management	Probable etiology of acute bronchitis; microorganisms were isolated in PSB and TBAs or identified by seroconversion ^g
1	31.0	58.7	52.8	Hospital ward, before ETI	18	NIV (duration, 3 h) ^f	Hemophilus influenzae
2	44.8	74.1	60.5	Hospital ward, before ETI	31	ETI, VC ventilation	Hemophilus influenzae
3	23.8	50.3	47.3	Emergency room, after ETI	27	VC ventilation	Hemophilus influenzae
4	28.1	46.8	60.0	Emergency room, after ETI	29	VC ventilation	Pseudomonas aeruginosa
5	21.7	44.7	48.6	Emergency room, after ETI	34	VC ventilation	Hemophilus influenzae, Enterobacter cloacae
6	42.3	81.6	51.8	Emergency room, after ETI	30	VC ventilation	Moraxella catarrhalis, Pseudomonas aeruginosa
7	26.4	48.0	55.0	Hospital ward, before ETI	27	ETI, VC ventilation	Moraxella catarrhalis, Influenza virus ^h
8	22.6	55.1	41.1	Emergency room, after ETI	27	VC ventilation	Streptococcus pneumoniae, Pseudomonas aeruginosa
9	39.8	63.6	62.5	Hospital ward, before ETI	28	NIV (duration, 2.5 h) ^f	Pseudomonas aeruginosa, Chlamydia pneumoniae ⁱ
10	29.8	44.4	67.0	Hospital ward, before ETI	28	NIV (duration, 1 h) ^f	Streptococcus pneumoniae

There were no patients with an already existing tracheostomy. The duration of mechanical ventilation until study protocol initiation ranged within 19.2–54.8 h. COPD = chronic obstructive pulmonary disease; HT = hypertension (primary); AF = atrial fibrillation; CVD = cerebrovascular disease; CAD = coronary artery disease; MD = major depression; DM = diabetes mellitus; OB = obesity; MAT = multifocal atrial tachycardia; PVD = peripheral vascular disease; FEV₁ and FVC = forced expiratory volume in 1 s and forced vital capacity, respectively (predicted values were those of Hankinson JL, Odencrantz JR, Fedan JB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999;159:178–87); ICU = intensive care unit; ETI = endotracheal intubation; APACHE = acute physiology and chronic health evaluation; NIV = noninvasive ventilation; VC = volume-controlled; PSB = protected specimen brush (cutoff value for positive microorganism isolation, 10² colony forming U/mL); TBAs = tracheobronchial aspirates (cutoff value for positive microorganism isolation, 10⁵ colony forming U/mL).

^a All patients were current or ex smokers. ^b Presented spirometric values were determined during the period of clinical stability that preceded the episode of acute bronchitis reported herein. ^c Asymptomatic on warfarin, digoxin, and verapamil. ^d Diagnosed with the Geriatric Mental State Schedule. ^e Previous history of stress-related, recurrent episodes, which were responsive to IV magnesium. ^f Ventilator settings were inspired O₂ fraction of 0.30–0.60; pressure support level of 15–20 cm H₂O, and positive end-expiratory pressure of 5–10 cm H₂O. ^g Defined as at least four-fold increase in serum immunoglobulin (Ig) G titer. ^h Seroconversion as just defined was considered as diagnostic. ⁱ Seroconversion as just defined reaching a titer of ≥1:512 or a serum IgM titer of ≥1:32 was considered as diagnostic.

inotropes, antipyretics, vasodilators, antiarrhythmic treatment, diuretics, insulin, or bronchodilators would cause patient exclusion. Electrocardiographic lead II, peripheral intraarterial, and pulmonary artery (Hands off[®] Infusion Port Thermodilution Catheter, Arrow, Reading, PA) pressures, urinary bladder temperature (Mon-a-therm[™] Foley-Temp[™], Mallinckrodt, St Louis, MO), and peripheral O₂ saturation (So₂) were monitored continuously.

After replacement of any enteral nutrition by a parenteral of identical nutrient-composition and administration rate (with subsequent propofol infusion-related lipid intake taken into account), gastric contents' evacuation by suction, nasogastric tube removal, and hydroxyethyl starch administration (3–5 mL/kg), patients were placed in a baseline supine (supine_{BAS}) position (90 degree inclination). Anesthesia and neuromuscular blockade were induced and maintained throughout the

study period with propofol-fentanyl and cisatracurium, respectively. Full train-of-four inhibition (facial nerve stimulation) was always accomplished. Baseline ventilator settings (volume control mode) were: tidal volume (V_T) of 0.6 ± 0.02 L; breaths/min, 18.0 ± 0.7 ; inspiratory time-to-total respiratory cycle length ratio, 0.20 ± 0.01 ; inspiratory flow (V/s), 0.91 ± 0.02 L/s; plateau pressure time, 0 s; positive end-expiratory pressure (PEEP), 0 cm H_2O ; and F_{iO_2} , 0.6.

V/s was measured with a heated pneumotachograph and a differential pressure transducer, and V_T was obtained by V/s -signal integration (6). Tracheal pressure (Paw) was measured with a 1.5-mm ID, 50-cm long catheter placed 2–3 cm past the ETT-tip and a pressure transducer (6). Esophageal pressure (Pes) and gastric pressure (Pga) were measured with a thin-walled latex double balloon-catheter system (6); proximal and distal balloons were placed in the mid-esophagus and stomach and inflated with 0.5 and 1.0 mL of air, respectively. Each balloon-catheter was proximally connected to a pressure transducer (6). Correct esophageal balloon placement was verified just before the cisatracurium administration by occlusion test (7). Paw - Pes difference yielded transpulmonary pressure (PL). After analog-to-digital conversion (sample rate, 200 Hz), variable-data were stored on IBM-type computer hard disk for later-on-analysis with a dedicated program (2). Breathing circuit modifications were as previously described (6).

Respiratory mechanics were assessed with constant V/s rapid airway occlusion (6) in the supine_{BAS}, protocol supine (supine_{PROT}), semirecumbent (45 degree inclination), and prone positions. The latter three postures' order was randomized *a priori* for all 10 patients with the Research Randomizer (<http://www.randomizer.org/form.htm>). Patients remained in each posture for 65–75 min. Supine-to-prone and prone-to-supine turning were performed by six attendants with an ETT and pressure-measuring devices manually immobilized and temporarily disconnected from breathing circuit (for ≤ 20 s) and pressure transducers, respectively. After patient turning, ETT displacement was excluded by capnography, breath sound auscultation, and unchanged insertion length-confirmation (used also for exclusion of pressure-measuring devices displacement). After pronation, abdominal movement-restriction was minimized (2).

Apart from nonbaseline test breaths, described later, only previously described baseline ventilation was used. In supine_{BAS} position, a pair of test breaths (V_T , 0.6 L [baseline]; square-wave V/s , 0.91 L/s) were administered within 45–55 min after neuromuscular blockade institution. Within 45–65 min after assumption of each studied posture, test breaths with constant, square-wave V/s (0.91 L/s) and V_T randomly varied from baseline to 0.2, 0.4,

0.8, 1.0, and 1.2 (sigh) L were administered twice. Test breaths were separated by brief baseline ventilation periods (Fig. 1) (6).

For each rs component, variables were abbreviated as "defined variable abbreviation, rs component" (e.g., cw-intrinsic PEEP [PEEPi] or PEEPi,cw).

Baseline-ventilation PEEPi,rs was measured as the Paw -plateau during the test breath preceding ~ 2 -s end-expiratory occlusion (EEO) referred to atmospheric pressure (Fig. 1). PEEPi,L, PEEPi,cw, and abdominal cw-component (PEEPi,ab-cw) were measured as respective EEO-plateau pressures referred to their preocclusion values (8). PEEPi,ab-cw was always approximately zero. End-expiratory lung volume (EELV)-change ($\Delta EELV$) was measured as previously described (6).

EEO was followed by 4 to 5-s end-inspiratory occlusion (EIO), enabling determination of maximal pressure (P_{max}), pressure immediately after EIO-initiation (P_1), and plateau pressure (P_2) during Paw - Pes computer-stored-data display, and of P_{max} and P_2 during Pga computer-stored-data display (Fig. 1). In accordance with PEEPi determinations, Paw values were referred to atmospheric pressure, whereas Pes - Pga values were referred to their pre-EEO values (6,8). During EIO, Paw was unaffected by gas exchange (6).

1.2-L- V_T test breaths were used as sigh breaths, which constitute effective recruitment maneuvers (3); other recruitment maneuvers were not used. According to randomized posture sequence, pronation was used immediately after supine_{BAS} in three patients, to whom pre-prone sigh breaths were not administered. Sigh breaths were to be discontinued if P_2aw exceeded 45 cm H_2O (9). High F_{iO_2} was selected because of possible participation of nonresponders to pronation (10) and to minimize hypoxemia-risk during $\Delta EELV$ determinations and hemodynamic measurements. Any pronation-induced hypoxemia ($SO_2 \leq 90\%$) would result in protocol termination and body posture-ventilatory variable change.

In each posture, intravascular-pressure transducers (Abbott, Sligo, Ireland) were zeroed at right atrial level. Within 30–45 min after posture assumption, thermodilution cardiac output (CO), central venous pressure (CVP), and pulmonary artery wedge pressure (PAWP) were determined three times consecutively during respective 30 to 45-s ETT disconnections from breathing circuit. ETT disconnections were initiated at end-inspiration and separated by two 5-min-lasting baseline ventilation intervals. Accordingly, heart rate and mean arterial blood pressure and MPAP values were averaged over each ETT-disconnection period. Just before each ETT disconnection, mixed venous and arterial

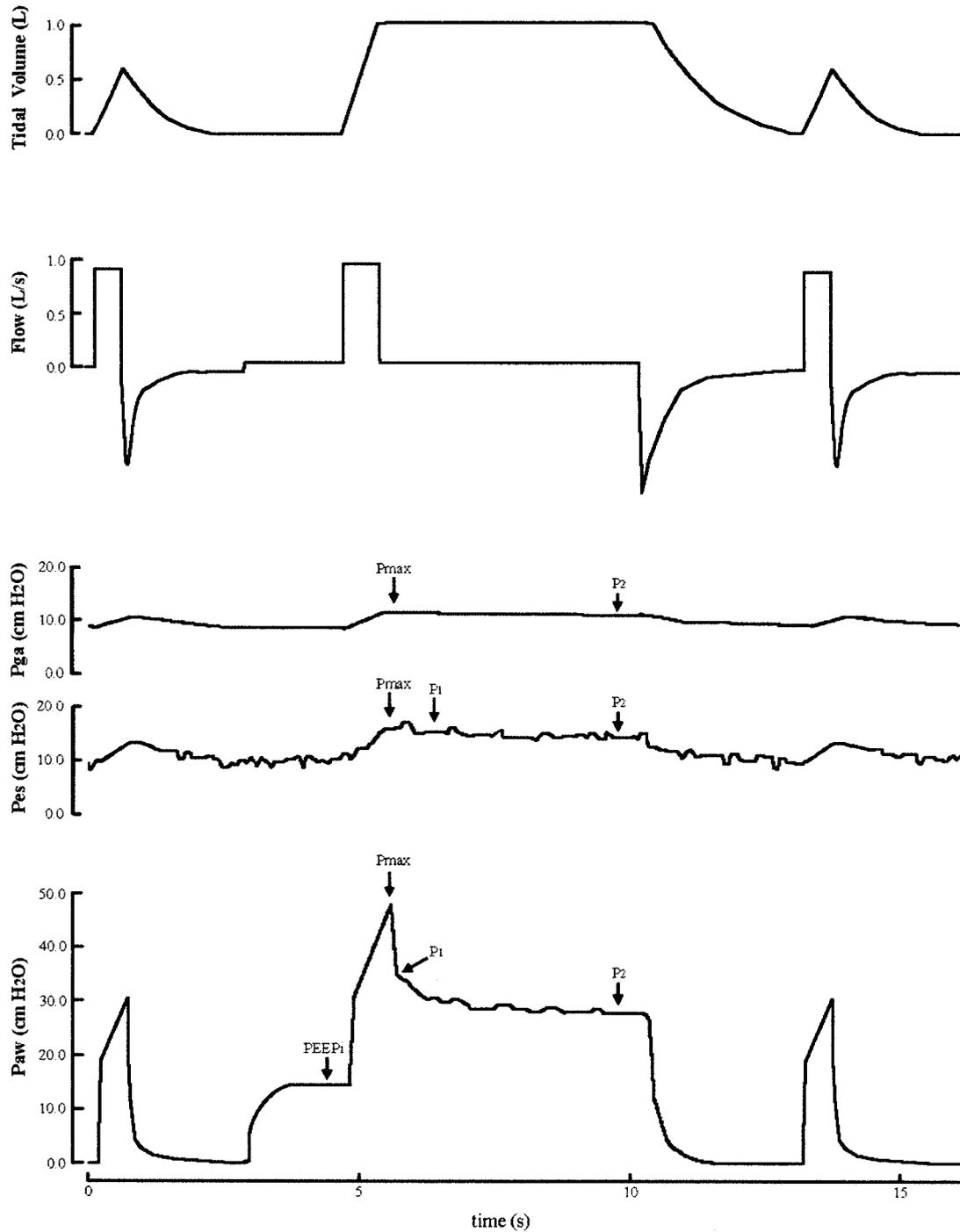


Figure 1. Tidal volume, inspiratory flow, and gastric (Pga), esophageal (Pes), and tracheal pressure (Paw) print-out of computer-stored-data display showing two baseline ventilation mechanical breaths (tidal volume = 0.6 L) separated by a test breath (tidal volume = 1.0 L). The presented variable-data originate from a representative study participant. The 1.88-s end-expiratory and the 4.60-s end-inspiratory airway occlusion (EIO) were performed before and just after the administration of the 1.0 L tidal volume, respectively. Note that on the displayed Pes tracing, characteristic perturbations caused by cardiac wall motion (i.e., cardiac oscillations) are present. Thus, Pmax was measured at the brief plateau preceding the first post-EIO cardiac oscillation, whereas P₁ was measured at the brief plateau in-between the first and second post-EIO cardiac oscillation. The maximal amplitude of each EIO-oscillation was determined as the difference between oscillation's peak Pes-value and preceding plateau Pes-value. For each EIO-oscillation, Pes-increase rate was defined as Pes-change from preceding plateau-to-peak value over time. In the presented test breath, Pes-increase rate was determinable in the 1st, 2nd, 3rd, 4th, and 6th post-EIO oscillations (83%), because they were preceded by clearly identifiable plateaus. The same methodology was used in the analysis of all stored Pes-data. Pes-increase rate was determinable in $\geq 67\%$ of EIO-oscillations of each analyzed test breath. PEEP_i = intrinsic positive end-expiratory pressure; Pmax = peak inspiratory pressure; P₁ = pressure immediately after end-inspiratory airway occlusion; P₂ = plateau inspiratory pressure.

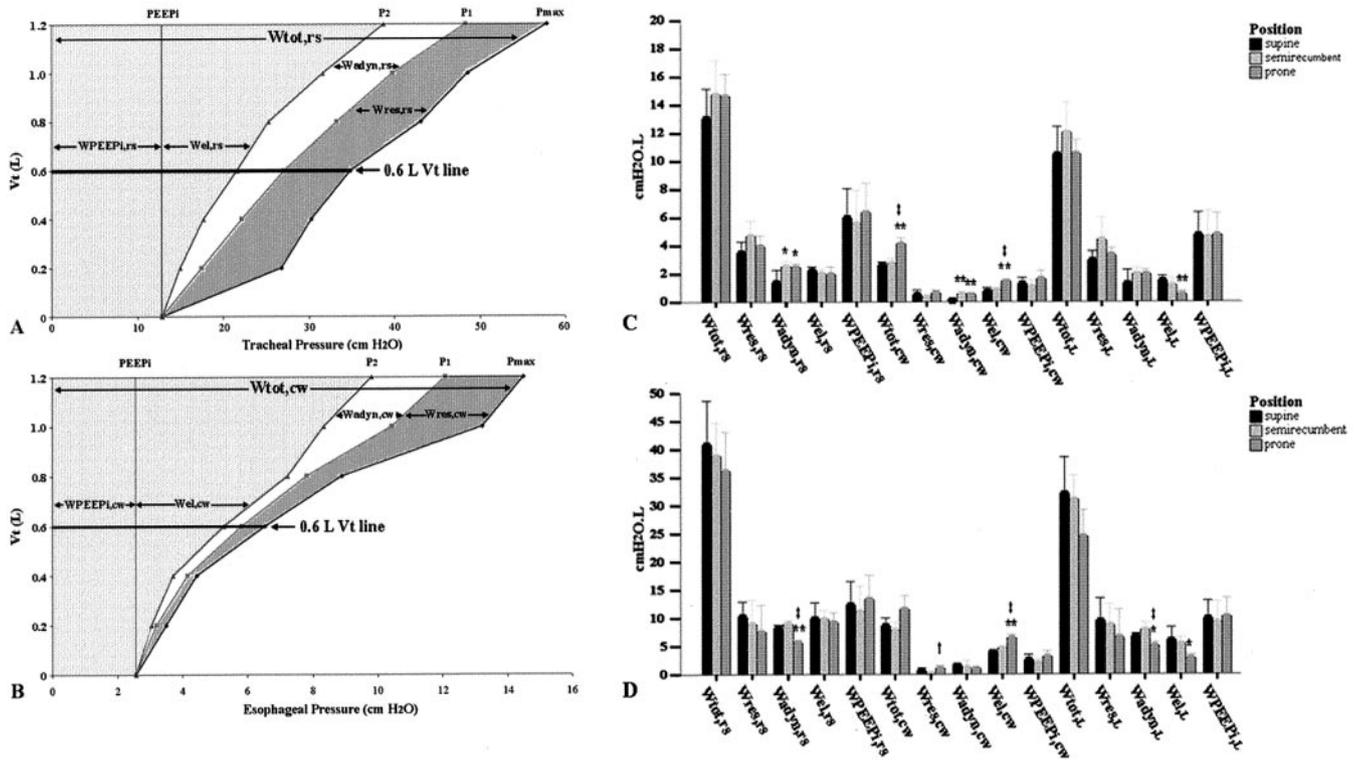


Figure 2. Methodology of determination of the static and dynamic components of the inspiratory work performed on the respiratory system (rs) (A) and chest wall (cw) (B) of a representative study participant; inspiratory work comparison-results at 0.6 L and 1.2 L inflation volume (V_T) (C and D, respectively). (A and B) Work components corresponding to 0.6 L V_T were determined by measuring the respective highlighted areas enclosed by the tracheal (A) and esophageal (B) pressure-volume curves labeled P_{max}, P₁, P₂, and PEEP_i, the volume and pressure axes, and the 0.6 L V_T lines. Work components corresponding to 1.2 L V_T were determined by measuring the respective highlighted total areas subtended by the aforementioned pressure-volume curves. (C and D) Bars show mean values, and error bars show mean + SD. Comparison-results of inspiratory work subcomponents (measurement-unit, cm H₂O · L) were thoroughly consistent in terms of presence of significant differences with the comparison-results of the rs, cw, and lung (L) mechanical properties they reflect (see also Appendix II and Results; Table 2; Figs. 3A,B,E,F). In the presented figure, inspiratory work subcomponents of each rs component are abbreviated as defined work subcomponent abbreviation, rs component (e.g., total work [W_{tot}] of the rs, W_{tot,rs}). P_{max} = peak inspiratory pressure; P₁ = pressure immediately after end-inspiratory airway occlusion; P₂ = plateau inspiratory pressure; PEEP_i = intrinsic positive end-expiratory pressure; W_{tot} = total work; W_{res} = resistive work, W_{adyn} = additional dynamic work; W_{el} = elastic work; WPEEP_i = work due to PEEP_i. */** = significantly different versus protocol supine, P < 0.05 / < 0.01 (respectively); † / ‡ = significantly different versus semirecumbent, P < 0.05 / < 0.01 (respectively).

blood gas (BG) samples were taken and analyzed immediately (ABL System 625; Radiometer, Copenhagen, Denmark). There were no appreciable differences among initial, second, and third BG values. Thus, BG analyses corresponded to baseline ventilation conditions. BG temperature corrections were not performed. Only BG analysis-derived SO₂ values were analyzed. Formula-derived variables included cardiac, systemic and pulmonary vascular resistance index, O₂ consumption ($\dot{V}O_2$), respiratory quotient (R), alveolar PO₂, and shunt fraction (Q_S/Q_T) (Appendix I). For each posture, only means of variable value-sets were analyzed.

V/s, V_T, Paw, Pes, and Pga values of test breath-pairs were stored and averaged in Microsoft Excel 2000. The following variable sets were determined at baseline and sigh V_T: (a) maximal (R_{max}), ohmic (R_{min}), and additional (ΔR) rs-component resistances (defined as corresponding P_{max}-P₂, P_{max}-

P₁, and P₁-P₂ differences divided by preceding V/s, respectively) and (b) dynamic (E_{dyn}), static (E_{stat}), and additional (ΔE) rs-component elastances (defined as corresponding P₁-PEEP_i, P₂-PEEP_i, and P₁-P₂ differences divided by preceding V_T, respectively). For the three protocol postures, pressure-volume curves were constructed, and total (W_{tot}), resistive, additional dynamic, elastic, and PEEP_i inspiratory work per breath performed on each rs component were determined by respective surface area measurement in Autocad 2000 (Autodesk, San Rafael, CA) (Figs. 2A and B).

Variable-comparisons among body postures were conducted with repeated-measures analysis of variance, followed by Scheffé test for *post hoc* comparisons whenever appropriate. Significance was set at P < 0.05. Values are presented as mean ± SD or grand mean* ± SD. Statistical analysis was performed with SPSS 10.0 (SPSS Inc., Chicago, IL).

Table 2. Respiratory System, Chest Wall, and Lung Mechanics During Baseline Ventilation (inflation volume = 0.6 L) and Sigh-Equivalent (inflation volume = 1.2 L) Test Breaths and Corresponding Ventilatory Variables

Baseline breath: V_T (L), 0.6 ± 0.01; f/min, 18.0 ± 0.4; T_i (s), 0.66 ± 0.02; V/s (L/s), 0.91 ± 0.01; EEO time (s), -2; EIO time (s), 4-5; PEEP_e (cm H₂O), 0

Position, rs component	R _{max} (cm H ₂ O/L/s)	R _{min} (cm H ₂ O/L/s)	ΔR (cmH ₂ O/L/s)	Edyn (cm H ₂ O/L)	Estat (cm H ₂ O/L)	ΔE (cm H ₂ O/L)	PEEP _i (cm H ₂ O)
Baseline supine, rs	14.3 ± 3.0	9.1 ± 2.7	5.2 ± 1.0	23.8 ± 1.9	16.0 ± 1.9	7.9 ± 1.6	9.5 ± 3.1
Baseline supine, cw	1.4 ± 0.7	0.8 ± 0.3	0.6 ± 0.4	6.0 ± 1.0	5.2 ± 1.0	0.9 ± 0.6	2.1 ± 0.8
Baseline supine, L	12.9 ± 2.4	8.3 ± 2.5	4.6 ± 1.1	17.8 ± 1.9	10.8 ± 1.7	7.0 ± 1.6	7.4 ± 2.4
Protocol supine, rs	14.1 ± 2.5	9.2 ± 2.6	4.9 ± 1.0	22.1 ± 2.8	14.7 ± 3.1	7.4 ± 1.5	9.9 ± 3.5
Protocol supine, cw	1.5 ± 0.6	0.9 ± 0.3	0.6 ± 0.4	6.1 ± 0.9	5.2 ± 0.9	0.9 ± 0.6	2.1 ± 0.8
Protocol supine, L	12.6 ± 2.1	8.3 ± 2.4	4.3 ± 1.0	16.0 ± 3.4	9.5 ± 3.2	6.5 ± 1.6	7.8 ± 2.9
Semirecumbent, rs	19.2 ± 2.8 †	11.5 ± 2.4	7.7 ± 1.3 †	26.2 ± 3.2	14.5 ± 3.1	11.7 ± 2.0 †	9.3 ± 3.9
Semirecumbent, cw	2.5 ± 0.6	0.8 ± 0.3	1.6 ± 0.6 †	8.2 ± 0.7 †	5.8 ± 0.6	2.5 ± 1.0 †	1.7 ± 0.7
Semirecumbent, L	16.7 ± 2.4	10.7 ± 2.5	6.1 ± 1.1	17.9 ± 3.2	8.7 ± 2.7	9.2 ± 1.6	7.6 ± 3.2
Prone, total rs	17.2 ± 3.5	9.7 ± 3.8	7.5 ± 0.5 †	25.8 ± 2.7	14.4 ± 2.2	11.4 ± 0.8 †	10.5 ± 3.9
Prone, cw	2.6 ± 1.0	1.1 ± 0.5	1.5 ± 0.5 †	10.7 ± 0.7 ††	8.4 ± 0.9 ††	2.3 ± 0.8 †	2.7 ± 1.0
Prone, L	14.2 ± 2.9	8.6 ± 3.5	6.0 ± 1.0	15.1 ± 2.4	6.0 ± 1.4§*	9.1 ± 1.4	7.9 ± 2.4

Sigh breath: V_T (L), 1.2 ± 0.02; f/min, 9.0 ± 0.2; T_i (s), 1.33 ± 0.03; V/s (L/s), 0.91 ± 0.02; EEO time (s), -2; EIO time (s), 4-5; PEEP_e (cm H₂O), 0

Position, rs component	R _{max} (cm H ₂ O/L/s)	R _{min} (cm H ₂ O/L/s)	ΔR (cmH ₂ O/L/s)	Edyn (cm H ₂ O/L)	Estat (cm H ₂ O/L)	ΔE (cm H ₂ O/L)	PEEP _i (cm H ₂ O)
Protocol supine, rs	18.6 ± 2.5	10.5 ± 1.1	8.1 ± 1.6	27.5 ± 3.0	21.4 ± 2.6	6.1 ± 1.2	10.3 ± 3.5
Protocol supine, cw	3.8 ± 1.4	0.8 ± 0.3	3.1 ± 1.0	7.6 ± 1.1	5.3 ± 0.5	2.3 ± 0.8	2.1 ± 0.8
Protocol supine, L	14.7 ± 2.5	9.8 ± 1.3	5.0 ± 1.5	19.8 ± 2.0	16.1 ± 2.3	3.8 ± 1.1	8.2 ± 2.7
Semirecumbent, rs	18.4 ± 2.7	9.3 ± 0.2	9.1 ± 2.6	26.4 ± 4.6	19.6 ± 3.2	6.9 ± 2.0	9.4 ± 3.9
Semirecumbent, cw	2.6 ± 0.7	0.5 ± 0.2	2.1 ± 0.7	8.1 ± 1.4	6.6 ± 1.3	1.6 ± 0.6	1.7 ± 0.7
Semirecumbent, L	15.8 ± 2.7	8.8 ± 0.2	7.0 ± 2.7	18.3 ± 3.3	13.0 ± 2.8	5.3 ± 2.0	7.7 ± 3.2
Prone, total rs	12.1 ± 2.3††	9.1 ± 2.0	3.0 ± 1.3††	23.8 ± 1.7	21.6 ± 2.2	2.3 ± 1.0††	11.1 ± 3.6
Prone, cw	3.2 ± 2.0	1.5 ± 0.6†	1.7 ± 1.5	11.7 ± 1.3††	10.4 ± 0.8††	1.3 ± 1.2	2.6 ± 0.9
Prone, L	8.9 ± 1.3	7.6 ± 1.7	1.3 ± 1.1*†	12.2 ± 1.3††	11.1 ± 1.4*	1.0 ± 0.9*†	8.5 ± 2.7

Values are mean ± SD.

V_T, inflation volume; f/min, ventilatory rate; T_i, inspiratory time; V/s, inspiratory flow; EEO, end-expiratory occlusion; EIO, end-inspiratory occlusion; PEEP_e, externally applied positive end-expiratory pressure; rs, respiratory system; cw, chest wall; L, lung; R_{max}, maximal (total) resistance; R_{min}, ohmic resistance; ΔR, additional resistance; Edyn, dynamic elastance; Estat, static elastance; ΔE, additional elastance; PEEP_i, intrinsic positive end-expiratory pressure.

* P < 0.05 significantly different versus protocol supine; † P < 0.01 significantly different versus protocol supine; ‡ P < 0.01 significantly different versus semirecumbent; § P < 0.05 significantly different versus baseline supine; || P < 0.01 significantly different versus baseline supine.

Results

Full data were obtained from all patients, and no protocol-related complications (e.g., pneumothorax-atelectasis, extubation-catheter removal, or patient injury) (10) occurred. Sigh breath P_{2aw} never exceeded 41.0 cm H₂O. Nine patients were weaned from mechanical ventilation at 4.9 ± 1.0 days and discharged from the hospital 5.7 ± 1.2 days thereafter; one died of sepsis.

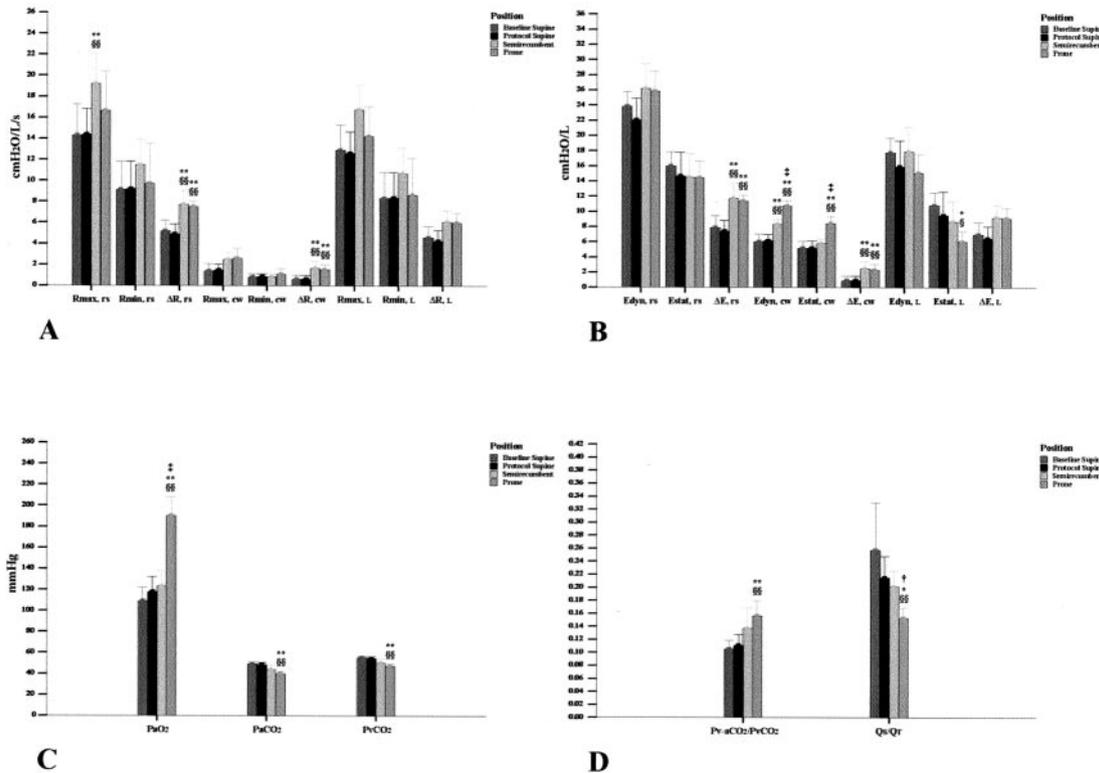
At baseline V_T, prone positioning resulted in (a) higher Edyn,cw and Estat,cw versus all other postures (all P < 0.01), and (b) higher ΔR,rs, ΔE,rs, ΔR,cw, and ΔE,cw and lower Estat,L versus supine_{BAS} and supine_{PROT} (P < 0.05-0.01); semirecumbent positioning resulted in higher Rmax,rs, ΔR,rs, ΔE,rs, ΔR,cw, Edyn,cw, and ΔE,cw versus supine_{BAS} and supine_{PROT} (all P < 0.01) (Table 2; Figs. 3A,B,E,F). At sigh V_T, prone positioning resulted in (a) lower Rmax,rs, ΔR,rs, ΔE,rs, ΔR,L, and ΔE,L and higher Edyn,cw and Estat,cw versus supine_{PROT} and semirecumbent (P < 0.05-0.01), (b) higher Rmin,cw versus semirecumbent (P < 0.01), and (c) lower Estat,L versus supine_{PROT} (P < 0.05). Inspiratory work comparison-results were

consistent with our results on elastance, resistance, and PEEP_i (Appendix II; Figs. 2C and D). W_{tot,rs}, which reflected total rs-impedance to mechanical breathing while V_T increased from 0.2 L to sigh (Appendix II; Fig. 2A), was unaffected by posture change (Figs. 2C and D).

No significant changes were observed in ΔEELV (0.41* ± 0.08 L), ΔP_{max,ga} at baseline and sigh V_T (3.8* ± 1.0 and 6.3* ± 3.6 cm H₂O, respectively), and ΔP_{2,ga} at baseline and sigh V_T (3.4* ± 0.8 and 4.9* ± 3.8 cm H₂O, respectively). Thus, body posture did not affect dynamic hyperinflation (6), R_{max,ab-cw}, and Estat,ab-cw. P_{ga} at rs relaxation volume (V_r) (11.1* ± 4.9 cm H₂O) was also unaffected by posture change, suggesting lack of prone position-related abdominal compression.

Pes at EELV (pre-EEO value) and V_r were lower in prone versus supine_{BAS} and supine_{PROT} positions (10.7 ± 2.1 and 6.1 ± 1.5 versus 17.8 ± 3.5 and 16.9 ± 3.0 and 13.3 ± 4.0 and 10.6 ± 1.8 cm H₂O, respectively; all P < 0.05), indicating lack of comparability of absolute Pes-measurements. Pes at EELV exceeded Pes at

Tidal Volume = 0.6 L



Tidal Volume = 1.2 L

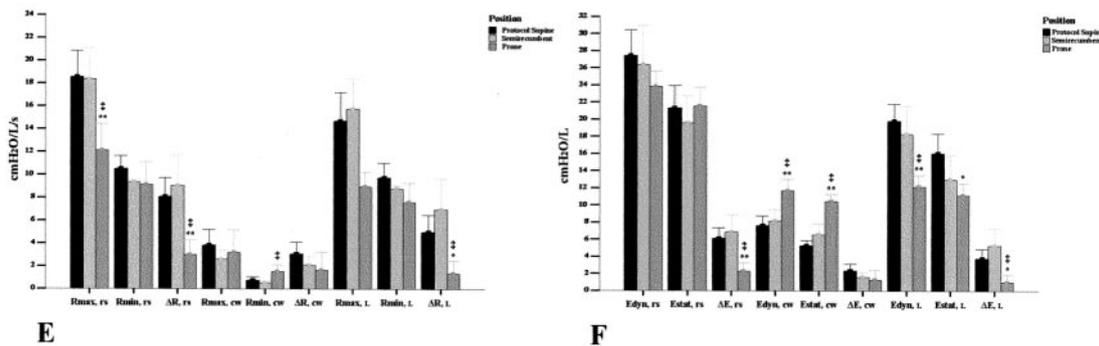


Figure 3. Results on resistance, elastance, and gas exchange obtained from the whole study group. Bars show mean values, and error bars show mean + SD; precise numerical values are given in Tables 2 and 3. The presentation includes only variables that exhibited at least one posture change-related significant change (Tables 2 and 3). (A-D) Results on resistance, elastance, blood gases, and CO₂ elimination and shunt fraction (respectively) obtained at baseline (0.6 L) tidal volume; (E and F) results on resistance and elastance (respectively) obtained at sigh (1.2 L) tidal volume. rs = respiratory system; cw = chest wall; L = lung; Rmax = maximal (total) resistance; Rmin = ohmic resistance; ΔR = additional resistance because of tissue stress relaxation tension and/or L-time constant inequalities; Edyn = dynamic elastance; Estat = static elastance; ΔE = additional elastance due to tissue stress relaxation tension and/or L-time constant inequalities; Pa = arterial gas partial pressure; Pv = mixed venous gas partial pressure; Pv-a = mixed venous-to-arterial gas partial pressure difference; Q_S/Q_T = shunt fraction. In the presented figure, elastance and resistance variables of each rs-component are abbreviated as already defined variable abbreviation, rs component (e.g., maximal [total] resistance [Rmax] of the rs, Rmax,rs). §/§§ = significantly different versus baseline supine, *P* < 0.05/< 0.01 (respectively); */** = significantly different versus protocol supine, *P* < 0.05/< 0.01 (respectively); †/‡ = significantly different versus semirecumbent, *P* < 0.05/< 0.01 (respectively).

Table 3. Hemodynamics and gas exchange. Gas exchange results correspond to baseline ventilation conditions (see also Methods)

Hemodynamic variables										
Body posture	HR (beats/min)	MAP (mm Hg)	CVP (mm Hg)	MPAP (mm Hg)	PAWP (mm Hg)	CI (L·min·m ⁻²)	SvO ₂ (%)	VO ₂ (mL·min·m ⁻²)	SVRI (dynes·s·cm ⁵ ·m ⁻²)	PVRI (dynes·s·cm ⁵ ·m ⁻²)
Baseline supine	86 ± 9	81 ± 11	9 ± 2	24 ± 3	13 ± 2	4.1 ± 0.4	82 ± 2	140 ± 19	1412 ± 286	209 ± 51
Protocol supine	86 ± 9	81 ± 10	9 ± 2	24 ± 3	14 ± 2	4.2 ± 0.5	82 ± 2	142 ± 19	1388 ± 268	203 ± 47
Semirecumbent	93 ± 9	78 ± 10	9 ± 2	23 ± 3	12 ± 2	4.1 ± 0.5	82 ± 2	143 ± 20	1367 ± 288	206 ± 51
Prone	89 ± 7	80 ± 9	9 ± 2	25 ± 4	13 ± 2	4.2 ± 0.5	82 ± 2	146 ± 21	1369 ± 286	216 ± 59

Gas exchange data									
Body posture	PaO ₂ (mm Hg)	Paco ₂ (mm Hg)	pHa	PvO ₂ (mm Hg)	Pvco ₂ (mm Hg)	pHv	Q _s /Q _T	Pv-aco ₂ /Pvco ₂	
Baseline supine	109 ± 13	49.5 ± 1.5	7.41 ± 0.06	49.8 ± 3.4	55.2 ± 1.5	7.38 ± 0.05	0.26 ± 0.07	0.10 ± 0.01	
Protocol supine	118 ± 14	48.5 ± 2.0	7.42 ± 0.07	51.5 ± 4.3	54.4 ± 1.9	7.38 ± 0.05	0.22 ± 0.03	0.11 ± 0.02	
Semirecumbent	123 ± 15	43.5 ± 4.5	7.44 ± 0.06	51.4 ± 4.2	50.3 ± 3.7	7.39 ± 0.04	0.20 ± 0.02	0.14 ± 0.03	
Prone	190 ± 18 ‡	40.0 ± 2.0 †	7.45 ± 0.05	52.0 ± 3.5	47.4 ± 2.0	7.39 ± 0.04	0.15 ± 0.02 *	0.16 ± 0.02 †	

Values are mean ± SD. Inspired O₂ fraction was 0.6.
 HR = heart rate; MAP = mean arterial blood pressure; CVP = central venous pressure; MPAP = mean pulmonary artery pressure; PAWP = pulmonary artery wedge pressure; CI = cardiac index; SvO₂ = mixed venous oxygen saturation; VO₂ = oxygen consumption; SVRI = systemic vascular resistance index; PVRI = pulmonary vascular resistance index; Pa = arterial partial pressure; pHa = arterial pH; Pv = mixed venous partial pressure; pHv = mixed venous pH; Q_s/Q_T = shunt fraction; Pv-a = mixed venous-arterial partial pressure difference.
 * *P* < 0.05 significantly different versus protocol supine; † *P* < 0.01 significantly different versus protocol supine; ‡ *P* < 0.01 significantly different versus semirecumbent; § *P* < 0.05 significantly different versus semirecumbent; || *P* < 0.01 significantly different versus baseline supine.

Vr in all postures (all *P* < 0.05 by paired *t*-test). By selecting the larger of these two expiratory Pes-values as reference (see Methods), we eliminated the effect of their posture-related variability on our determinations of test breath-induced changes in Pes (8).

During EIO, mean maximal amplitude of cardiac oscillations in Pes (Fig. 1) was similar in all postures (1.4* ± 0.6 cm H₂O), indicating similar magnitude of transmitted intracardiac pressure-changes to the esophageal balloon. During EIO-oscillations, mean Pes-increase rate (Fig. 1) was also stable (9.0* ± 3.2 cm H₂O/s) in all postures.

Posture changes did not affect hemodynamic variables. In contrast, pronation resulted in (a) higher PaO₂ and lower Q_s/Q_T versus all other postures (*P* < 0.05–0.01) and (b) lower Paco₂ and mixed venous Pco₂ (Pvco₂) versus supine_{BAS} and supine_{PROT} (all *P* < 0.01) (Table 3; Figs. 3C and D).

During study period, there were no appreciable changes in energy expenditure or metabolic rate determinants such as physiologic stress level (clinical stability was maintained), patient-temperature (37.3* ± 0.4, maximal fluctuation always ≤0.6°C), feeding, and medication. Also, formula-derived V̇O₂ was stable and calculated R constant; thus, CO₂ production should also be stable. During study period, CO was stable, indicating unchanged CO₂-delivery rate to the Ls and time available for alveolar-capillary gas equilibration. Consequently, in each posture, mixed venous-to-arterial CO₂ concentration difference (Cv-aco₂) reflected L-CO₂ elimination efficiency. Because CCO₂-Pco₂ relationship was almost linear at rest and

its determinants (pH, HCO₃, hemoglobin concentration, and So₂) (11) were unaffected by posture change, similar Pco₂ changes reflected similar CCO₂ changes in all postures. Furthermore, in each posture, mixed venous-to-arterial Pco₂ difference (Pv-aco₂) reflected L-CO₂ elimination efficiency in that particular posture (12). However, as L-CO₂ excretion also depends on Pvco₂ *per se* (12), we expressed its efficiency as fractional Pvco₂ change after the blood passes through the pulmonary circulation (Pv-aco₂/Pvco₂). Pv-aco₂ and Pvco₂ were higher in prone position versus supine_{BAS} and supine_{PROT} (both *P* < 0.01).

Random posture sequence resulted in five patients being repositioned supine after pronation (Table 4; Fig. 4). Regarding cw mechanics, prone versus supine_{BAS} and supine_{POSTPRO} differences were as previously described (Tables 2 and 4; Figs. 3A and B, 4A and B); however, Estat,L was lower only versus supine_{BAS} (*P* < 0.01). Accordingly, supine_{POSTPRO} versus supine_{BAS} resulted in lower Estat,rs and Estat,L (*P* < 0.05–0.01). Regarding CO₂, prone versus supine_{BAS} and supine_{POSTPRO} differences were as previously described (Tables 3 and 4; Figs. 3C and D, 4C and D). However, Q_s/Q_T was similar in the prone position and supine_{POSTPRO}. Accordingly, supine_{POSTPRO} versus supine_{BAS} resulted in lower Q_s/Q_T and higher PaO₂ (*P* < 0.05–0.01). By contrast, in the five patients in whom supine_{PROT} preceded pronation (supine_{PREPRO}), all supine_{BAS} and supine_{PREPRO} versus prone differences in rs mechanics and gas exchange were as above for the whole patient group (data not shown).

Table 4. Baseline Supine, Postprone Supine, and Prone Respiratory Mechanics During Baseline Ventilation Test Breaths (see also Methods and Table 2) and Gas Exchange Data in Five Study Participants. Gas Exchange Data Correspond to Baseline Ventilation Conditions (see also Methods, Table 2, and Figs. 4C and D)

Respiratory mechanics							
Position, rs component	Rmax (cm H ₂ O/L/s)	Rmin (cm H ₂ O/L/s)	ΔR (cmH ₂ O/L/s)	Edyn (cm H ₂ O/L)	Estat (cm H ₂ O/L)	ΔE (cm H ₂ O/L)	PEEPi (cm H ₂ O)
Baseline supine, rs	16.6 ± 2.2	10.9 ± 2.6	5.6 ± 0.9	24.9 ± 2.1	16.4 ± 1.6	8.6 ± 1.3	11.9 ± 1.9
Baseline supine, cw	1.8 ± 0.7	1.0 ± 0.3	0.8 ± 0.5	6.8 ± 0.8	5.6 ± 0.9	1.2 ± 0.8	2.5 ± 0.6
Baseline supine, L	14.8 ± 1.8	9.9 ± 2.5	4.9 ± 1.3	18.1 ± 2.7	10.8 ± 1.9	7.4 ± 2.0	9.4 ± 1.4
Postprone supine, rs	16.0 ± 2.0	11.0 ± 2.4	5.0 ± 0.9	20.1 ± 2.5	12.6 ± 1.8§	7.5 ± 1.4	12.6 ± 2.1
Postprone supine, cw	1.8 ± 0.5	1.0 ± 0.2	0.8 ± 0.4	6.8 ± 0.5	5.6 ± 0.9	1.2 ± 0.7	2.5 ± 0.7
Postprone supine, L	14.1 ± 1.5	9.9 ± 2.3	4.2 ± 1.2	13.3 ± 2.5	7.0 ± 1.2§	6.3 ± 1.9	10.1 ± 1.5
Prone, rs	20.0 ± 1.0	12.7 ± 1.5	7.2 ± 0.5‡*	24.4 ± 0.9	13.4 ± 0.8	11.0 ± 0.8‡‡	13.1 ± 2.0
Prone, cw	3.2 ± 1.0	1.3 ± 0.6	1.9 ± 0.6‡*	10.9 ± 0.5‡§	8.0 ± 0.6‡§	2.8 ± 0.7‡*	3.4 ± 0.6
Prone, L	16.8 ± 0.1	11.4 ± 0.9	5.3 ± 0.8	13.5 ± 1.0	5.4 ± 0.5§	8.2 ± 1.3	9.7 ± 1.4

Gas exchange data						
Position	Pao ₂ (mm Hg)	Paco ₂ (mm Hg)	Pvo ₂ (mm Hg)	Pvco ₂ (mm Hg)	Q _S /Q _T	Pv-aco ₂ /Pvco ₂
Baseline supine	104 ± 12	50.4 ± 1.3	49.1 ± 2.3	56.0 ± 0.9	0.28 ± 0.07	0.10 ± 0.02
Postprone supine	130 ± 5§	46.7 ± 0.6	52.9 ± 3.8	52.7 ± 0.7	0.18 ± 0.03‡	0.12 ± 0.02
Prone	204 ± 11‡§	38.3 ± 0.9‡§	52.2 ± 3.4	45.8 ± 0.7‡§	0.14 ± 0.03§	0.17 ± 0.03§*

Values are mean ± SD. Results on hemodynamics and pH are omitted because they were similar to those presented in Table 3.
rs = respiratory system; cw = chest wall; L = lung; Rmax = maximal (total) resistance; Rmin = ohmic resistance; ΔR = additional resistance; Edyn = dynamic elastance; Estat = static elastance; ΔE = additional elastance; PEEPi = intrinsic positive end-expiratory pressure; Pa = arterial partial pressure; Pv = mixed venous partial pressure; Q_S/Q_T = shunt fraction; Pv-a = mixed venous-arterial partial pressure difference.
* P < 0.05 significantly different versus postprone supine; † P < 0.01 significantly different versus postprone supine; ‡ P < 0.05 significantly different versus baseline supine; § P < 0.01 significantly different versus baseline supine.

Discussion

Our main findings were: (a) at baseline V_T, pronation increases Edyn,cw and Estat,cw and improves arterial oxygenation and Q_S/Q_T versus supine and semirecumbent, whereas it also decreases Estat,L and augments CO₂ excretion versus supine, (b) regarding L-mechanics at sigh V_T, pronation also decreases L-tissue stress relaxation tension and L-time constant inequality (Appendix II) versus supine and semirecumbent positions, (c) in abdominal compression absence, posture change (and especially pronation) does not affect hemodynamic status, (d) W_{tot,rs} and, thus, overall mechanical ventilation conditions (see Results and Appendix II) are unaffected by posture change, and (e) regarding Estat,L, arterial oxygenation, and Q_S/Q_T, pronation-related benefits versus supine_{BAS} seem to be maintained in supine_{POSTPRO} for at least 30–65 min, whereas the reverse is true for CO₂ elimination.

We showed that semirecumbent positioning merely increases thoracic-tissue viscoelastic resistance versus supine at baseline V_T (Appendix II; Tables 2 and 3; Figs. 2C and D, 3A); nevertheless, its major benefit versus supine is reduction of nosocomial pneumonia risk (13). In contrast, pronation augments ventilation-perfusion (V/Q) matching and CO₂ elimination versus supine; probable contributory factors include increased ribcage elastance (2) and elimination of

L-compression by the heart (14), resulting in decreased Estat,L, attenuated L-inflation gradient, and more homogenous regional and increased total effective alveolar ventilation (V_{ALV}) versus supine (2,14). Pronation proved superior versus semirecumbent with respect to V/Q matching but not CO₂ elimination; this is consistent with the cw/L mechanics similarities in semirecumbent and supine positions but suggests a slightly increased effective V_{ALV} in the former.

In supine_{POSTPRO}, CO₂ elimination decreased toward baseline (Table 4, Figs. 4C and D), indicating accentuated L-inflation gradient versus prone, causing a decrease in effective V_{ALV}; accordingly, cw mechanics were similar versus supine_{BAS}; however, arterial oxygenation and Q_S/Q_T were still improved versus supine_{BAS} (Table 4, Figs. 4C and D), indicating partial maintenance of pronations augmented V_{ALV} homogeneity and V/Q matching; this is consistent with enhanced dorsal L-region recruitment during tidal L-inflation versus supine_{BAS} because of the preceding pronation effects (2).

Some may argue that our results on pronation were mainly because of posture change-induced mobilization of tracheobronchial secretions. However, this cannot explain the partial reversal of pronation benefits in supine_{POSTPRO} because they should be further enhanced by further secretion mobilization secondary to further posture change.

Tidal Volume = 0.6 L

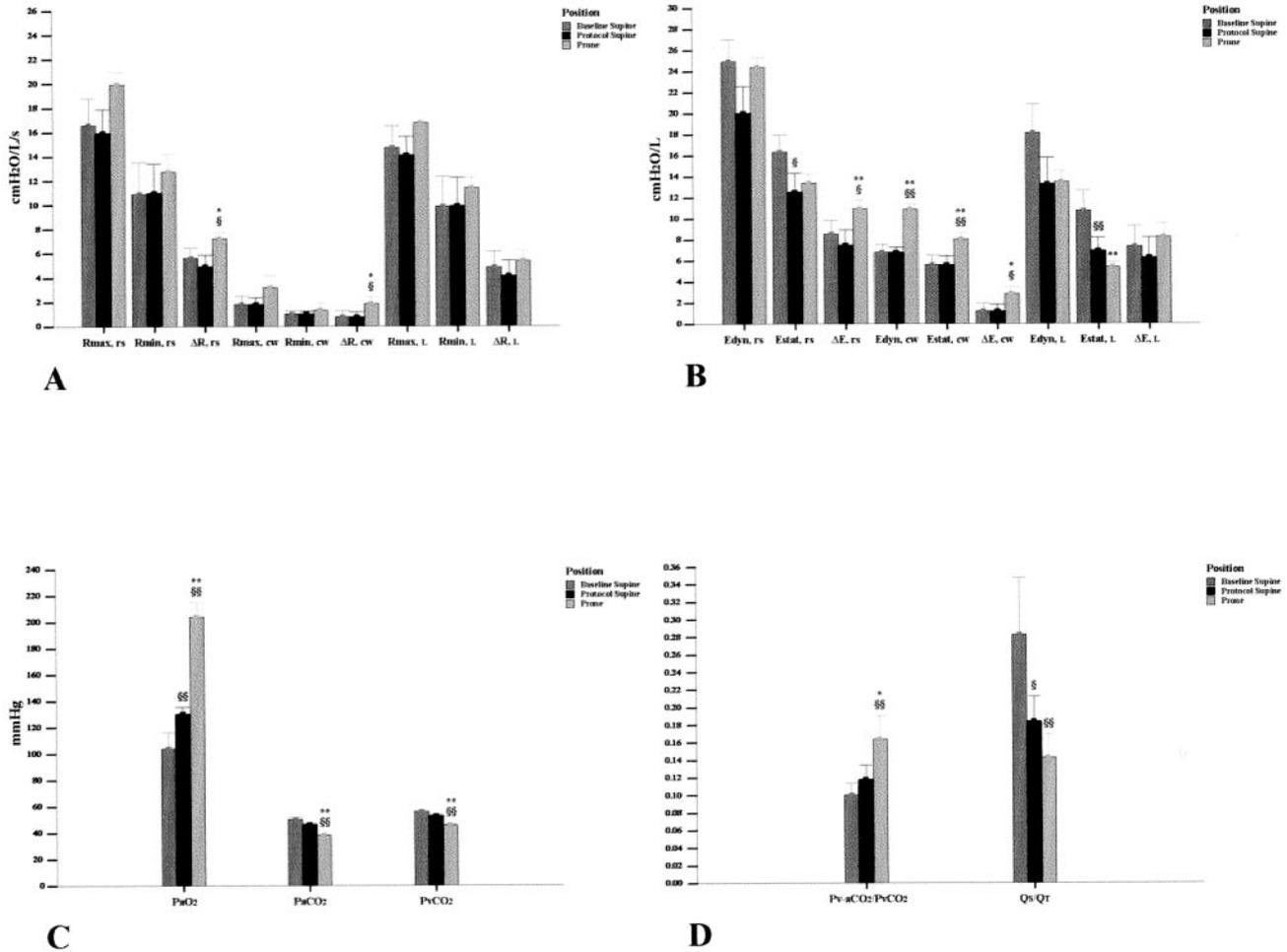


Figure 4. Results on resistance, elastance, and gas exchange obtained from the postprone supine subgroup. Bars show mean values, and error bars show mean + SD; precise numerical values are given in Table 4. The presentation includes only variables that exhibited at least one posture shift-related significant change in the whole study group and the aforementioned subgroup (Tables 2-4; Fig. 3). (A-D) Results on resistance, elastance, blood gases, and CO₂ elimination and shunt fraction (respectively) obtained at baseline (0.6 L) tidal volume. rs = respiratory system; cw = chest wall; L = lung; Rmax = maximal (total) resistance; Rmin = ohmic resistance; ΔR = additional resistance due to tissue stress relaxation tension or L-time constant inequalities; Edyn = dynamic elastance; Estat = static elastance; ΔE = additional elastance due to tissue stress relaxation tension or L-time constant inequalities; Pa = arterial gas partial pressure; Pv = mixed venous gas partial pressure; Pv-a = mixed venous-to-arterial gas partial pressure difference; Q_s/Q_T = shunt fraction. In the presented figure, elastance and resistance variables of each rs-component are abbreviated as already defined variable abbreviation, rs component (e.g., maximal [total] resistance [Rmax] of the rs, Rmax,rs). §/§§ = significantly different versus baseline supine, *P* < 0.05/< 0.01 (respectively); */** = significantly different versus protocol supine, *P* < 0.05/< 0.01 (respectively).

The pronation-induced reduction in L-time constant inequality during sigh-V_T EIO (Appendix II; Table 2; Figs. 2D, 3E and F) suggests a reduced number of L-units with very low (tending toward 0) or high (tending toward infinity) time constants and, thus, a reduced number of atelectatic and hyperinflated alveoli, respectively; this further suggests increased sigh effectiveness and reduced alveolar-rupture probability. Furthermore, the observed hemodynamic and ventilation-conditions' stability and absence of posture-shift-related complications in conjunction

with the rest of our results demonstrate prone position's applicability, effectiveness, and benefits versus semirecumbent positioning.

Posture sequence randomization enabled posture-data determinations and comparisons without risk of a certain posture order systematically influencing results obtained in a subsequent one. Data on a postsemirecumbent supine position were not obtained for comparison with our postprone data; however, available and presented data (Table 2; Fig. 3) strongly suggest lack of semirecumbent-related

benefit after supine posture resumption. Consequently, our methodology has enabled us to produce results leading to satisfactory conclusions regarding pronation merits.

Pes-measurements reliability could be questionable because after pronation, alveolar pressure transmission to the esophagus may vary as the heart moves ventrally (2). A change in heart positioning relative to the esophagus or esophageal-balloon should also affect transmission of intracardiac pressure changes to the latter. However, myocardial wall motion pattern, contractility, and cyclic intracardiac pressure changes should have remained stable in all postures (see Results; Table 3); consequently, our EIO-cardiac oscillation data suggest unchanged transmission pattern of intracardiac pressure changes to the esophageal balloon. Thus, the initial correct esophageal-balloon positioning relative to the heart was probably maintained throughout the study period, and respiratory cycle-induced Pes-changes were measured as accurately as possible in all postures (2,15).

A severe limitation was that no systematic data collection was planned in supine_{POSTPRO} position. This was counterbalanced by posture random order resulting in available-for-comparison supine_{POSTPRO} data in five participants. Because all determined variables exhibited similar response-patterns to posture change in all supine_{POSTPRO}-subset members, it is unlikely that the small size of the latter had significantly affected the results (16); this is also true for the whole study group. However, we cannot totally exclude type II errors (2).

EELV, physiologic and alveolar dead space and energy expenditure were not directly determined. The former two limitations were partially counterbalanced by our determinations of Δ EELV (increment in functional residual capacity because of expiratory flow limitation) (6) and $P_v\text{-aCO}_2/P_v\text{CO}_2$ (which reflected effective V_{ALV} during hemodynamic and probable metabolic stability) (see Results). Finally, O_2 measurements with metabolic monitors may exhibit inaccuracies at $F_{IO_2} > 0.5$ (17).

Noninvasive positive-pressure ventilation (NIPPV) is recommended as first-line treatment in ARF-COPD patients (18-21). NIPPV may avert invasive mechanical ventilation (IMV) in 50%-75% of cooperative, alert, hemodynamically stable patients (18-21). However, a meta-analysis (22) revealed an overall NIPPV-induced IMV-reduction of only 18% in an ARF-COPD cohort, originating from 15 randomized-controlled trials (RCTs). Also, approximately 80% of ARF-COPD patients admitted to a university-affiliated intensive care unit required IMV (23). ARF-COPD patients exhibit an in-hospital mortality of 24% (24), which may be reduced by using lower V_{rs} during IMV (and thus, decreasing the incidence of hemodynamic compromise and ventilator-induced lung injury [VILI]) (23). Interestingly, recent evidence suggests that intermittent pronation may also

reduce VILI-risk (25). Our findings of pronation-induced improvement in L-mechanical behavior (Table 2; Figs. 3A,B,E,F) are consistent with reduced VILI risk; furthermore, we demonstrated a pronation-induced improvement in gas exchange efficiency (i.e., L-function) (Tables 2 and 3; Figs. 3C and D), partially maintained along with pronation Estat,L-reduction (improvement in L-mechanics) in supine_{POSTPRO} (Table 4; Figs. 4A-D). Thus, pronation may constitute a useful therapeutic strategy in the management of ARF-COPD patients, and RCTs comparing outcomes of COPD patients treated with prone and semirecumbent positioning are warranted.

Appendix I

Formulas used to derive hemodynamic and gas exchange variables¹

1. Cardiac index = CO/BSA.
2. Systemic vascular resistance index = (MAP-CVP) · 80/CI.
3. Pulmonary vascular resistance index = (MPAP-PAWP) · 80/CI.
4. O_2 consumption per m^2 BSA = CI · 1.36 · Hgb · (Sao₂-Svo₂).
5. Respiratory quotient = (FEY of carbohydrate intake) · 1.0 + (FEY of protein intake) · 0.8 + (FEY of lipid intake) · 0.7.²
6. Alveolar Po₂ = P_{IO₂} - P_ACO₂ · (F_{IO₂} - (1-F_{IO₂}) · R⁻¹); P_{IO₂} = F_{IO₂} · (P_B-47); P_ACO₂ ~ P_aCO₂.
7. O_2 content of blood = Hgb · 1.36 · SO₂/10 + 0.003 · Po₂.
8. Shunt fraction = (CCO₂-CaO₂)/(CCO₂-CvO₂).

CO = cardiac output (L/min); BSA = body surface area (m²); MAP = mean arterial blood pressure (mm Hg); CVP = central venous pressure (mm Hg); CI = cardiac index (L · min⁻¹ · m⁻²); 80 = transformation factor of Wood units (mm Hg · L⁻¹ · min) to standard metric units (dynes · s · cm⁻⁵); MPAP = mean pulmonary artery blood pressure (mm Hg); PAWP, pulmonary artery wedge pressure (mm Hg); Hgb = hemoglobin concentration in g/L; 1.36 = O₂ combining power of 1 g of hemoglobin (mL); Sao₂ = arterial O₂ saturation; Svo₂ = mixed venous O₂ saturation; FEY = fractional energy yield relative to total of pre-scribed nutritional support; P = gas partial pressure (mm Hg); P_{IO₂} = inspired O₂ partial pressure (mm Hg); P_ACO₂ = alveolar CO₂ partial pressure (mm Hg); F_{IO₂} = inspired O₂ fraction; R = respiratory quotient; P_B =

¹ Sources: Mark JB, Slaughter TF, Reves JG. Cardiovascular monitoring. In: Miller RD, ed. Anesthesia. 5th ed. New York: Churchill Livingstone, 2000:1117-230, and Moon ME, Camporesi EM. Respiratory monitoring. In: Miller RD, ed. Anesthesia. 5th ed. New York: Churchill Livingstone, 2000:1255-96.

² Source: Reference 17.

barometric pressure (mm Hg); 47 = water saturated vapor pressure at 37°C (mm Hg); 0.003 = O₂ solubility coefficient at 37°C (mL · dL⁻¹ · mm Hg); P_{O₂} = O₂ partial pressure (mm Hg); CcO₂/CaO₂/CvO₂ = O₂ content in end-capillary/arterial/mixed-venous blood (respectively).

Appendix II

*Relationships among inspiratory work subcomponents and elastance, resistance, and intrinsic positive end-expiratory pressure (PEEPi).*³

1. Total inspiratory work reflects in combination PEEPi during baseline mechanical ventilation (see Methods) and ohmic resistance (R_{min}), additional resistance (ΔR),⁴ caused by time constant inequality within the lung or tissue stress relaxation tension and static elastance (E_{stat}) as tidal volume varies from 0.2 to 1.2 L (by 0.2 L increments) with square-wave inspiratory flow kept constant at 0.91 L/s (protocol test breathing (PTB) described in Methods).

2. Resistive inspiratory work reflects R_{min} during PTB.

3. Additional dynamic work reflects ΔR and ΔE during PTB.

4. Elastic inspiratory work reflects E_{stat} during PTB.

5. PEEPi inspiratory work reflects PEEPi during baseline mechanical ventilation.

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³ Sources: Reference 6 and Eissa NT, Ranieri VM, Correil C, et al. Analysis of behavior of the respiratory system in ARDS patients: effects of flow, volume, and time. *J Appl Physiol* 1991;70:2719-29.

⁴ Related to additional elastance (ΔE) according to the following formula: ΔE = ΔR/inspiratory time.