Acute Effects of Sitting Out of Bed and Exercise on Lung Aeration and Oxygenation in Critically Ill Subjects

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BACKGROUND: Early mobilization during critical illness is safe and has beneficial effects on functional outcomes. However, its impact on pulmonary function has not been thoroughly explored. We hypothesized that a sitting position out of bed coupled with exercise could result in an improvement in oxygenation and lung aeration. METHODS: The study was conducted on a cohort of adult subjects within a week of their admission to an ICU. Subjects were transferred to a chair and undertook a 15-min session of exercise, either active or passive. Subjects in the control group were only transferred to a chair. Electrical impedance tomography, a reliable bedside technique monitoring regional lung aeration and the distribution of ventilation, was continuously performed, and blood gases were assessed at baseline and 20 min post-exercise. RESULTS: The cohort included 40 subjects, 17 of whom were mechanically ventilated and 23 spontaneously breathing. The control group for each modality consisted of 5 mechanically ventilated or 5 spontaneously breathing subjects. Mild hypoxemia was present in 45% of the spontaneously breathing cohort, whereas the mechanically ventilated subjects demonstrated moderate (50%) or severe (12%) hypoxemia. Compared with the control group, early mobilization induced a significant increase in lung aeration. In mechanically ventilated subjects, lung aeration increased, especially in the anterior lung regions (mean impedance [95% CI]: T1 (baseline in bed) = 1,265 [691–1,839]; T2 (chair sitting) = 2,003 [1,042–2,963]; T3 (exercise) = 1,619 [810 2,427]; T4 (post exercise in chair) = 2,320 [1,186–3,455]). In spontaneously breathing subjects, lung aeration increased mainly in the posterior lung regions (mean impedance [95% CI]: T1 = 380 [124–637]; T2 = 655 [226–1,084]; T3 = 621 [335–906]; T4 = 600 [340–860]). P_{aO_2}/F_{IO_2} increased, especially in subjects with lower P_{aO_2}/F_{IO_2} at baseline (< 200) (133 ± 31 to 158 ± 48, *P* = .041). CONCLUSIONS: For critically ill subjects, a sitting position and exercise increased lung aeration and were associated with an improvement in P_{aO_2}/F_{IO_2} in the more severely hypoxemic subjects. *Key words: early mobilization; exercise therapy; critically ill; alveolar recruitment; oxygenation; electrical impedance tomography.* [Respir Care 2021;66(2):253–262. © 2021 Daedalus Enterprises]

Introduction

Critical illness, mechanical ventilation, and prolonged immobilization are risk factors that are associated with both neuromuscular and respiratory complications in patients in the ICU.[1-4] The recumbent position in critically ill patients affects ventilation and pulmonary perfusion, decreasing lung volume, increasing airway resistance, and contributing to hypoxemia and the need for a high level of supplemental oxygen.[5-6] Early mobilization reduces the negative effects associated with bed rest.[7-9] However, the benefits of early

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mobilization on the respiratory system have been less well explored. Semi-recumbent positioning and being seated out of bed are safe in mechanically ventilated patients, without significant changes in respiratory or hemodynamic parameters.[10,11] A seated position in bed between 45° and 60° increases lung volume and generates significant benefits in terms of oxygenation and end-expiratory lung volume in patients with ARDS.[12,13] Vertically positioning mechanically ventilated patients by standing or with a tilt-table induces a transitory increase in ventilation without significant modifications in oxygenation.[14,15] Early standing and ambulation in abdominal postoperative patients prevents postoperative pulmonary complications.[15-17] Various activities, such as bedside or in-chair cycling and even walking, are currently performed by many critically ill patients, and the impact of these activities on respiratory dynamics needs to be investigated.

The aim of this study was to use electrical impedance tomography (EIT) to investigate the acute pulmonary effects of sitting in a chair, coupled with different physical activities, on critically ill subjects. EIT is a noninvasive tool that enables bedside visualization of lung aeration by measuring electrical impedance in a cross-section of the thorax.[18,19] EIT has shown good accuracy and validity, correlating with other techniques[20]; notably, changes in end-expiratory lung impedance (EELI), measured with EIT, are highly correlated with changes in end-expiratory lung volume,[21] and the tidal variation of impedance has a strong correlation with tidal volume[22] that supports the use of these parameters. This technique has been used in ICUs to assess regional changes in ventilation in patients with ARDS, providing information on recruitment capacity and optimal individual PEEP titration.[23] We hypothesized that positioning a patient in a chair results in an improvement of lung aeration and oxygenation, especially when this position is combined with exercise.

Methods

Study Setting and Subject Allocation

This was a prospective study conducted in a mixed ICU at Saint-Luc University Hospital in Brussels, Belgium. Patients scheduled for early mobilization either undergoing invasive mechanical ventilation (eg, endotracheal tube or tracheostomy) or not undergoing invasive mechanical ventilation (ie, spontaneously breathing subjects) were eligible for enrollment in the study. Exclusion criteria were minors, agitation, major hemodynamic instability, length of ICU stay > 1 week, absence of consent, and technical limitations for EIT monitoring (eg, cardiac electric device, morbid obesity, or chest bandages[20]). Protocol approbation was obtained by the local biomedical ethics committee.

QUICK LOOK

Current knowledge

Critically ill patients have an increased risk of developing functional and respiratory complications. Physical activity is safe and has beneficial effects on several clinical outcomes in the critically ill.

What this paper contributes to our knowledge

A sitting position coupled with physical activity, such as cycling or walking, induced an increase in lung aeration as assessed with electrical impedance tomography in mechanically ventilated and spontaneously breathing subjects. P_{aO_2}/F_{IO_2} changes indicated that the greatest benefits of this intervention occurred in more severely hypoxemic subjects, independent of the use of mechanical ventilation. Physical activity was not detrimental to critically ill subjects; it did not induce adverse events, hypoxemic changes, or negative effects on lung aeration, and the subjects enjoyed the activity.

Outcomes

Our primary end point was lung aeration changes assessed using EIT in the overall thoracic section as well as posterior and anterior lung regions. As secondary end points, we assessed tidal impedance variation, homogeneity of ventilation, oxygenation changes and their correlation with ventilation assessed with EIT, hemodynamic tolerance, and subjects' perception.

Early Mobilization-Session Development

The mechanically ventilated subjects performed a leg cycle-ergometer session in a passive or active manner depending on their individual capacity. The spontaneously breathing subjects performed randomly assigned active exercises, either walking in place or using a motorized active leg or arm cycle-ergometer device (MOTOmed viva2, RECK-Technik Betzenweiler, Germany). During active cycling, resistance was individually adjusted according to subject tolerance. During walking, subjects were

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assisted so that they could achieve a standing position with a walker device and could maintain 15 min of continuous steps in place, according to their tolerance.

In both mechanically ventilated and spontaneously breathing subjects, the protocol was performed in 4 consecutive stages: (1) baseline (T1) – subjects stayed in bed (30° inclination); (2) in chair (T2) – subjects were transferred into a chair (70° inclination); (3) exercise (T3) – subjects undertook exercise for 15 min; and (4) post-exercise rest (T4) for 20 min in the chair.

To assess the isolated effect of chair sitting without exercise, subjects performing only the transfer into the chair were included as a nonexercise control group. Control groups were assessed at baseline (T1) and during their 45 min in the chair (T2–T4).

EIT Assessment

EIT monitoring was performed using the PulmoVista 500 (Dräger Medical, Lübeck, Germany). A thoracic belt with 16 electrodes was placed on the fourth intercostal space and kept in place during the entire measurement protocol. Conscious subjects were asked not to speak and to limit trunk movements during the recording period. Continuous EIT monitoring was performed, and bio-impedance records were extracted as follows: in the exercise groups, 5 min during both T1 and T2, 15 min during activity (T3), and 20 min during T4; in the control groups, 5 min during T1 and continuously during 45 min of sitting (T2–T4).

The bio-impedance values of each respiratory cycle were extracted using the EIT Data Analysis Tool 6.1 (Dräger Medical). The lower level of the respiratory cycle loop represents EELI. Changes in EELI are linearly correlated with changes in end-expiratory lung volume ($r^2 = 0.98$) and reflects alveolar recruitment. [21] In contrast, the magnitude of the lung impedance changes from the lower to the maximum level of each respiratory cycle loop (tidal impedance variation) are linearly correlated with lung tidal volumes ($r^2 = 0.97$) and reflect ventilation variations.[22] Numerical values of impedance have been expressed in arbitrary units, ranging from negative to positive numbers, with a huge variability among subjects' values. For this reason, and to evaluate the individual change during each stage, EIT impedance values for stages T2–T4 have been expressed as a ratio of T1 for each subject. The value of T1 is 1.0, and every ratio to this value is marked as a fold change of basal impedance values. Analyses were conducted involving the global thoracic region and separated into the anterior and posterior regions of interest (ROIs).[24] As previously described,[24] the homogeneity of the antero-posterior distribution of tidal volume was assessed by means of the ratio of ventilation variation on anterior to posterior ROIs, meaning that lower levels (near 1.0) represent better homogeneity of ventilation. Because of the position changes from bed to chair during our intervention, this analysis does not enable us to refer to dependent or nondependent ROIs, as proposed by Mauri et al[24]; we refer instead to anterior and posterior ROIs.

Clinical Parameters

Respiratory and hemodynamic parameters were recorded during each protocol stage. Arterial blood gases were collected at baseline (T1) and at the end of the post-exercise resting phase (T4). P_{aO_2}/F_{IO_2} was calculated using measured F_{IO_2} for mechanically ventilated subjects and for those receiving high-flow oxygen therapy, and it was estimated using tables for spontaneously breathing subjects.[25] A correlation between ventilation in the posterior ROIs and P_{aO_2}/F_{IO_2} was calculated.[24]

In subjects able to communicate, pain and exertion were evaluated before and after activity. Pain scores were monitored using a numeric scale ranging from 0 (no pain) to 10 (maximum pain),[26] and subject-perceived exertion was rated using a Borg scale (0–10).[27] Enjoyment was also evaluated at the end of activity using a similar 10-point rated scale (0 = no enjoyment, 10 = maximum enjoyment).[11]

Statistical Analyses

No specific sample size estimation was carried out because of a lack of previous reports and data in the literature. A convenience sample of consecutive subjects was enrolled during a 5-month period for subjects on mechanical ventilation and a 4-month period for spontaneously breathing subjects. Analyses were conducted using SPSS 21.0 (IBM, Armonk, New York) and plotted on graphs using GraphPad Prism 8 (GraphPad Software, La Jolla, California). Continuous variables were expressed as means with 95% CI or as medians with interquartile range. Because of right-skewed distributions, impedance values were log-transformed using a generalized logarithm before analysis, and its inverse, the hyperbolic sine transform, was used for reporting results. Such geometric means and geometric standard deviations are fold changes. Results were plotted in graphs using a multiplicative scale, and impedance values were reported in tables (see the supplementary materials at http://www.rcjournal.com). Categorical variables were analyzed with the chi-square test. Means or medians were compared between groups using the *t* test, the Mann-Whitney *U* test, and one-way analysis of variance with F or Kruskall-Wallis tests when appropriate. Linear and quadratic time trends were assessed and compared between groups using mixed models, with the group as a fixed factor and time as a random repeated factor with unequal spacing. For the strength of association between variables, Pearson correlation or Spearman rank correlation

Table 1. Demographic and Clinical Characteristics

	Mechanical Ventilation		*P*	Spontaneous Breathing		*P*
	Study Group	Control Group		Study Group	Control Group	
Subjects, *n*	17	5		23	5	
Age, y	68 ± 13	62 ± 18	.79	53 ± 15	55 ± 22	.59
Male	11 (65)	3 (60)	.99	13 (7)	4 (80)	.61
APACHE II score	23 ± 8	23 ± 6	.81	15 ± 6	19 ± 9	.63
SOFA score	9 ± 2	9 ± 2	.58	5 ± 3	4 ± 2	.50
ICU length of stay, d	14 ± 12	10 ± 7	.62	3 ± 3	3 ± 2	.81
Ventilation duration, h	6 ± 5	6 ± 6	.89	NR	NR	NR
28-d mortality	3 (18)	2 (40)	.54	0 (0)	0 (0)	> .99
Medical/surgical admission, %	88/12	100/0	.99	48/52	90/10	.042
Respiratory disease	10 (59)	2 (40)	.62	2 (9)	1 (20)	.45
Sepsis	2 (12)	2 (40)	.20	4 (17)	2 (40)	.28
Abdominal surgery	2 (12)	0 (0)	.99	12 (52)	1 (20)	.33
Digestive disease	1 (6)	0 (0)	.99	2 (9)	0 (0)	.99
Others	2 (12)	1 (20)	.99	3 (13)	1 (20)	.99
Berlin classification						
> 300 mm Hg	2 (12.5)	0 (0)	> .99	11 (50)	3 (75)	.60
Mild	4 (25)	2 (40)	.60	9 (41)	1 (25)	> .99
Moderate	8 (50)	3 (60)	> .99	1 (4.5)	0 (0)	> .99
Severe	2 (12.5)	0 (0)	> .99	1 (4.5)	0 (0)	> .99
ICU supports						
Vasopressors/inotropic	7 (41)	2 (40)	.99	NR	NR	NR
Sedatives	14 (82)	5 (100)	.99	NR	NR	NR
Opioid analgesics	5 (29)	4 (80)	.11	17 (74)	3 (60)	.60
Renal replacement therapy	1 (6)	1 (20)	.41	NR	NR	NR
At EIT evaluation						
RASS score	–1 ± 1	–1 ± 1	.87	0 ± 0	0 ± 0	NR
Ventilation duration, h	71 ± 62	83 ± 91	.75	NR	NR	NR
ICU length of stay, d	5 ± 3	5 ± 3	.56	1 ± 1	3 ± 3	.43

Data are presented as mean ± SD or *n* (%).
APACHE II = Acute Physiology and Chronic Health Evaluation II; SOFA = Sequential Organ Failure Assessment; NR = not reported; RASS = Richmond Agitation-Sedation Scale; EIT = electrical impedance tomography

coefficient was used, as appropriate. Intention-to-treat analyses were carried out using mixed models. All tests were 2-sided, and significance was set at the 0.05 probability level.

Results

Population Description

Overall, 24 mechanically ventilated subjects were included, while data from 7 subjects were excluded for the following reasons: 1 suffered from a persistent cough, 2 had hiccups, the exercise stage for 1 subject was interrupted by gastrointestinal activity, and 3 EIT records were dysfunctional. Seventeen mechanically ventilated subjects were analyzed as the mechanically ventilated group. In total, 34 consecutive spontaneously breathing subjects were included, while the records of 11 were excluded for the following reasons: 5 subjects were unable to sustain the requested exercise due to exhaustion, 1 subject presented with transient hypotension in a sitting position, and 6 EIT records were dysfunctional, including 1 subject who was unable to sustain the requested exercise. This allowed only 4 subjects to be included in the intention-to-treat analysis (see the supplementary materials at http://www.rcjournal.com). Overall, 23 spontaneously breathing subjects were analyzed (spontaneously breathing group). The control groups included 5 mechanically ventilated subjects (mechanically ventilated control) and 5 spontaneously breathing subjects (spontaneously breathing control).

Demographics and clinical characteristics are presented in Table 1. In the mechanically ventilated group, all subjects were ventilated by spontaneous modes of mechanical ventilation; 16 subjects were ventilated with pressure support ventilation, and 1 subject with proportional assist ventilation. The mean PEEP was 8 ± 3 cm H_2O with a mean F_{IO_2} of 0.41 ± 0.13%. The 5 subjects in

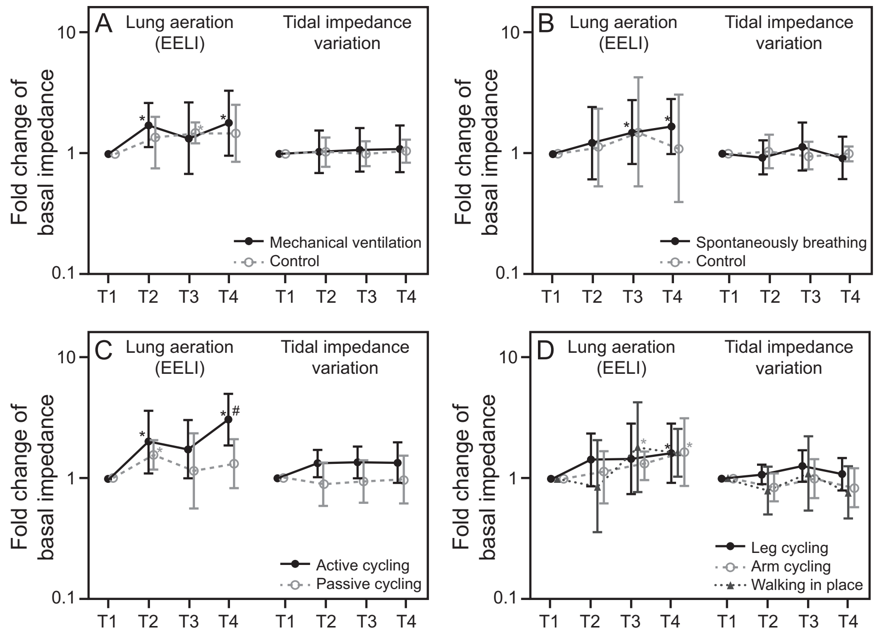

Fig. 1. Lung aeration and tidal impedance variations. A: Mechanically ventilated vs mechanically ventilated control. B: Spontaneously breathing vs spontaneously breathing control. C: Subgroup of mechanically ventilated subjects performing active leg cycling vs mechanically ventilated subjects performing passive leg cycling. D: Subgroups of spontaneously breathing subjects performing 3 different activities: leg cycling, arm cycling, and walking in place. Values are geometric means (geometric SD) and are fold changes of impedance from basal (T1 = reference) to T2, T3, and T4. T1 = baseline in bed; T2 = sitting in chair; T3 = exercising (resting in chair in control groups); and T4 = resting in chair. *Values are significant vs T1. #Values are significant between active and passive group. EELI = end-expiratory lung impedance.

the mechanically ventilated control group were ventilated with pressure support ventilation. The mean PEEP was 7 ± 3 cm H_2O ($P = .82$ compared with the mechanically ventilated group) with a mean F_{IO_2} of 0.37 ± 0.08% ($P = .50$ compared with the mechanically ventilated group). No subjects were tracheostomized or received noninvasive mechanical ventilation. In the spontaneously breathing group, 13 subjects needed oxygen support, 2 via high-flow oxygen therapy and 11 via a nasal cannula. Five subjects in the mechanically ventilated group had respiratory comorbidities: 4 had a diagnosis of COPD, and 1 subject had lung cancer. In the mechanically ventilated control group, 2 subjects had COPD. One subject in the spontaneously breathing group had a history of asthma, and 1 subject in the spontaneously breathing control group had COPD.

Early Mobilization Performance

In the mechanically ventilated group, 6 subjects performed active leg cycling on the cycle-ergometer, with a mean intensity of 2.9 ± 1.5 watts; the 11 remaining subjects performed passive leg cycling with a speed fixed at 20 rpm. In the spontaneously breathing group, 10 subjects performed leg cycling (mean intensity of 3.4 ± 0.5 watts), 7 performed arm cycling (mean intensity of 3.3 ± 0.5 watts), and 6 walked in place for 15 min.

Changes in Lung Aeration: EELI

In the mechanically ventilated group, the global EELI exhibited higher impedance values in the chair (T2) and during rest after exercise (T4) compared with baseline (T1) (mean impedance [95% CI]: T1 = 1,265 [691–1,839]; T2 = 2,003 [1,042–2,963]; T3 = 1,619 [810–2,427]; T4 = 2,320 [1,186–3,455]). In contrast, subjects in the mechanically ventilated control group displayed changes in EELI only during T2 (mean impedance [95% CI]: T1 = 750 [416–1,084); T2 = 973 [795–1,151]; T3 = 1,087 [731–1,443]; T4 = 1,142 [437–1,848]) (Fig. 1A and supplementary materials at http://www.rcjournal.com). In the spontaneously breathing group, EELI increased at T3 and T4 (mean impedance [95% CI]: T1 = 788 [551–1,025]; T2 = 1,040 [575–1,505]; T3 = 1,232 [649–1,815]; T4 = 1,312 [817–1,808]); in the spontaneously breathing control group, EELI showed no changes (mean impedance [95% CI]: T1 = 1,629 [–534 to 3,793], T2 = 1,475 [553–2,396]; T3 = 2,032 [962–3,103]; T4 = 1,702 [1,021–2,383]) (Fig. 1B and supplementary materials at http://www.rcjournal.com).

In the mechanically ventilated group, subjects' data were analyzed according to active or passive cycling exercise. An EELI increase was observed from T2 to T4 in active subjects ($n = 6$) (mean impedance [95% CI]: T1 = 680 [54–1,307]; T2 = 1,196 [258–2,134]; T3 = 994 [364–1,623]; T4 = 2,214 [11–4,417]). In contrast, passive

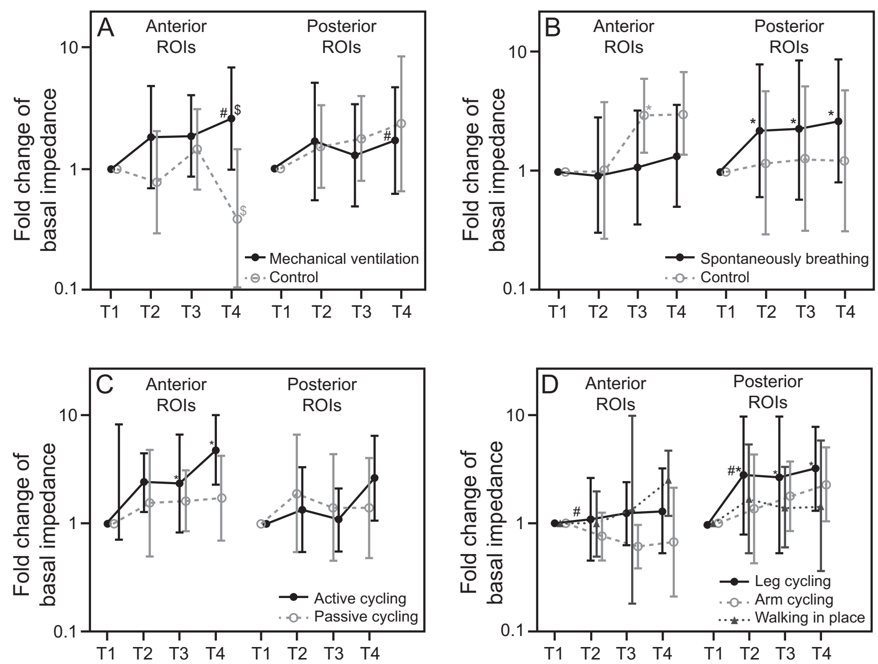

Fig. 2. Lung aeration in anterior and posterior ROIs. A: Mechanically ventilated vs mechanically ventilated control. B: Spontaneously breathing vs spontaneously breathing control. C: Subgroup of mechanically ventilated subjects performing active leg cycling vs mechanically ventilated subjects performing passive leg cycling. D: Subgroups of spontaneously breathing subjects performing three different activities: leg cycling, arm cycling, and walking in place. Values are geometric means (geometric SD) and are fold changes of impedance from basal (T1 = reference) to T2, T3, and T4. T1 = baseline in bed; T2 = sitting in chair; T3 = exercising (resting in chair in control groups); and T4 = resting in chair. *Values are significant vs T1. #Values are significant between anterior and posterior ROIs. $Values are significant between mechanically ventilated subjects and mechanically ventilated controls. ROI = region of interest.

subjects (n = 11) displayed an EELI increase only at T2 (mean impedance [95% CI]: T1 = 1,584 [762–2,407]; T2 = 2,443 [1,004–3,881]; T3 = 1,960 [719–3,201]; T4 = 2,378 [792–3,965]) (Fig. 1C and supplementary materials at http://www.rcjournal.com).

In a subgroup analysis of the spontaneously breathing group, which separated the 3 types of exercise (ie, leg cycling, arm cycling, and walking in place), EELI increases were observed at T3 for walking and in T4 for leg and arm cycling [(mean impedance for walking [95% CI]: T1 = 857 [–31 to 1,745]; T2 = 513 [182–844]; T3 = 1,072 [503–1,641]; T4 = 1,076 [416–1,736]); (mean impedance for leg cycling [95% CI]: T1 = 934 [628–1,240]; T2 = 1,640 [698–2,583]; T3 = 1,732 [371–3,092]; T4 = 1,761 [654–2,868]); and (mean impedance for arm cycling [95% CI]: T1 = 520 [221–820]; T2 = 635 [–7.07 to 1,277]; T3 = 655 [268–1,042]; T4 = 874 [383–1,366]) (Fig. 1D and supplementary materials at http://www.rcjournal.com). Any differences in EELI changes for the different types of exercise were detected.

Regarding the anterior and posterior EELI changes in the mechanically ventilated group and the mechanically ventilated control group, the mechanically ventilated group displayed higher impedances during T4 in anterior ROIs compared to the control group (mean impedance [95% CI]: T1 = 1,265 [691–1,839]; T2 = 2,003 [1,042–2,963]; T3 = 1,619 [810–2,427]; T4 = 2,320 [1,186–3,455] vs mean impedance for mechanically ventilated control group [95% CI]: T1 = 336 [111–564]; T2 = 295 [65–524]; T3 = 447 [293–601]; T4 = 140 [–213 to 493]) (Fig. 2A and supplementary materials at http://www.rcjournal.com). In the subgroup of the active mechanically ventilated group, EELI was increased in the anterior ROIs at T3 and T4 (mean impedance [95% CI]: T1 = 284 [0.3–568]; T2 = 620 [154–1,086]; T3 = 649 [241–1,056]; T4 = 1,308 [167–2,449]) (Fig. 2C and supplementary materials at http://www.rcjournal.com). This was in contrast to the spontaneously breathing group, in which EELI changes were clearly higher in the posterior ROIs from T2 to T4 (mean impedance [95% CI]: T1 = 380 [124–637]; T2 = 655 [226–1,084]; T3 = 621 [335–906]; T4 = 600 [340–860]) (Fig. 2B and supplementary materials at http://www.rcjournal.com). The spontaneously breathing control group displayed no differences between ROIs. In the subgroup of the spontaneously breathing group, the leg cycling group exhibited a greater increase in recruitment in the posterior ROIs compared with the anterior ROIs during T2 [(mean impedance anterior ROIs [95% CI]: T1 = 627 [323–931]; T2 = 610 [126–1,094]; T3 = 906 [121–1,690]; T4 = 926 [297–1,555]) vs (mean impedance posterior ROIs [95% CI]:

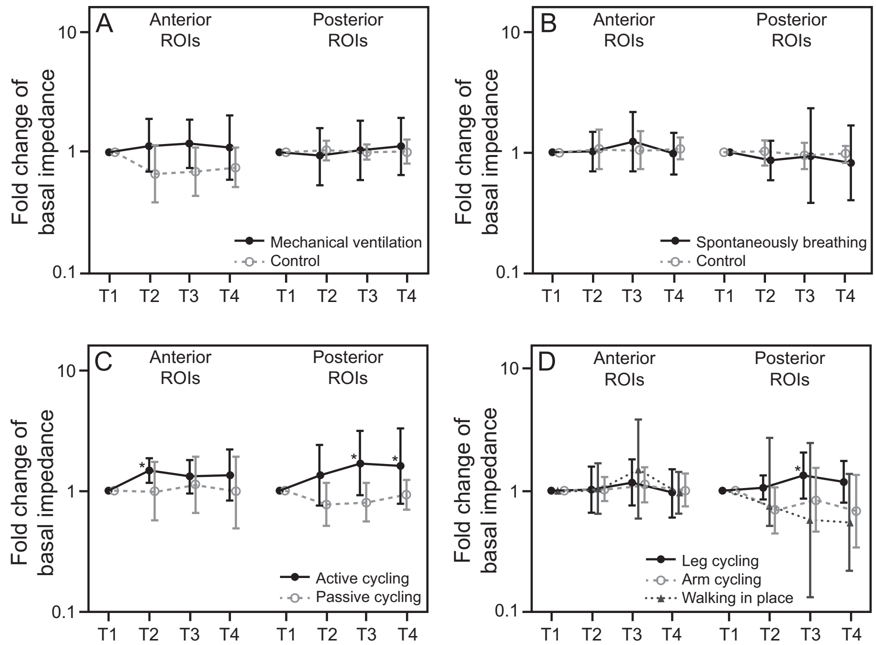

Fig. 3. Tidal impedance variations in anterior and posterior ROIs. A: Mechanically ventilated vs mechanically ventilated control. B: Spontaneously breathing vs spontaneously breathing control. C: Subgroup of mechanically ventilated subjects performing active leg cycling vs mechanically ventilated subjects performing passive leg cycling. D: Subgroups of spontaneously breathing subjects performing 3 different activities: leg cycling, arm cycling, and walking in place. Values are geometric means (geometric SD) and are fold changes of impedance from basal (T1 = reference) to T2, T3 and T4. T1 = baseline in bed; T2 = sitting in chair; T3 = exercising (resting in chair in control groups); and T4 = resting in chair. *Values are significant vs T1. ROI = region of interest.

T1 = 309 [23–595]; T2 = 1,030 [34–2,027]; T3 = 826 [202–1,451]; T4 = 834 [257–1,411])] (Fig. 2D and supplementary materials at http://www.rcjournal.com).

Changes in Tidal Impedance Variation and Homogeneity

Global tidal impedance variation assessed using EIT was not modified at any time or for any group (Fig. 1A–D and supplementary materials at http://www.rcjournal.com). Regarding the different ROIs, tidal impedance variation showed an increase only in the posterior ROIs of the active mechanically ventilated group at T3 and T4 (fold changes of impedance from basal [ie. geometric means (geometric SD)] (T1 = reference); T2 = 1.34 (1.79); T3 = 1.68 (1.84); T4 = 1.60 (2.03), $P = .01$) (Fig. 2C and supplementary materials at http://www.rcjournal.com). In the spontaneously breathing group, tidal impedance variation in the posterior ROIs increased at T3 during leg cycling (fold changes of impedance from basal (T1 = reference); T2 = 1.06 (1.26); T3 = 1.34 (1.55); T4 = 1.18 (1.48), $P = .01$). Similarly, subjects walking in place exhibited a tidal impedance variation increase in the anterior ROIs at T3 (fold changes of impedance from basal (T1 = reference); T2 = 1.03 (1.61); T3 = 1.50 (2.55); T4 = .95 (1.48), $P = .05$) (Fig. 3D and supplementary materials at http://www.rcjournal.com). Nonsignificant changes were found in the homogeneity index of regional ventilation during and after intervention, with the exception of the homogeneity calculated after leg cycling, in which a better homogeneity was found after exercise (T4) (homogeneity index [95% CI]; T1 = 1.12 [0.67–1.57]; T2 = 1.26 [0.53–1.98]; T3 = 0.99 [0.60–1.38]; T4 = 0.92 [0.61–1.24], $P = .02$) (see the supplementary materials at http://www.rcjournal.com).

Blood Gas Changes

No changes to F_{IO_2} were required during the protocol. P_{aO_2}/F_{IO_2} values of both the mechanically ventilated group and spontaneously breathing group increased from T1 to T4 (270 ± 119 to 287 ± 112, $P < .05$), contrasting with the overall control group (284 ± 95 to 287 ± 95, $P = .97$) (see the supplementary materials at http://www.rcjournal.com). In the spontaneously breathing group, the differences were maintained from 323 ± 110 to 347 ± 87 ($P = .01$), while the spontaneously breathing control group presented no variations (368 ± 70 to 357 ± 66, $P = .63$). In the mechanically ventilated group, this ratio remained unchanged (197 ± 91 to 203 ± 86, $P = .28$), which was similar to the mechanically ventilated control group ratio (218 ± 44 to 230 ± 75, $P = .81$). A positive correlation between P_{aO_2}/F_{IO_2} and tidal impedance variation in posterior

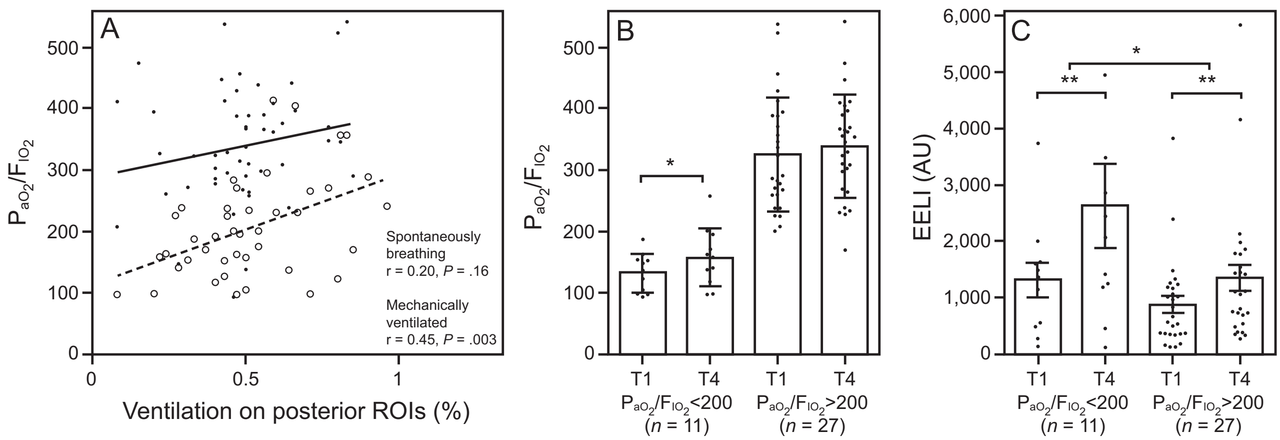

Fig. 4. P_{aO_2}/F_{IO_2} and EELI changes in subjects with baseline P_{aO_2}/F_{IO_2} lower or higher than 200. (A) P_{aO_2}/F_{IO_2} changes (T1 vs T4) in spontaneously breathing subjects and mechanically ventilated subjects with a T1 P_{aO_2}/F_{IO_2} of < 200 vs those with a P_{aO_2}/F_{IO_2} of ≥ 200; data expressed as mean ± SD. (B) EELI changes (T1 vs T4) in spontaneously breathing subjects and mechanically ventilated subjects with a T1 P_{aO_2}/F_{IO_2} of < 200 vs those with a P_{aO_2}/F_{IO_2} of ≥ 200; data expressed as median (interquartile range). T1 = baseline in bed, T4 = resting in chair after exercise. *P < .05, **P < .01. EELI = end-expiratory lung impedance; ROI = region of interest.

ROIs was found in subjects on mechanical ventilation (r = 0.45, *P* = .003), in contrast to spontaneously breathing subjects (r = 0.20, *P* = .16) (Fig. 4A). Interestingly, P_{aO_2}/F_{IO_2} (133 ± 31 to 158 ± 48, *P* = .041) and EELI benefits were larger in subjects with P_{aO_2}/F_{IO_2} < 200 at baseline, independent of the group (Fig. 4B, C). No variation in P_{aCO_2} was evidenced in any group (see the supplementary materials at http://www.rcjournal.com).

Respiratory and Hemodynamic Parameters

Oxygen saturation improved in all groups of subjects performing physical activities (see the supplementary materials at http://www.rcjournal.com). This increase was observed in the subgroup of subjects on mechanical ventilation during active leg cycling; in the spontaneously breathing group, the subjects doing active arm cycling presented a clear increase at T4. Breathing frequency was increased during each active exercise, returning, in most cases, to baseline values after exercise end. The increase in breathing frequency was accompanied by a slight decrease in tidal volume in the mechanically ventilated group during the active exercise, resulting in unmodified minute ventilation.

Heart rates were modified mainly during the active exercise in the spontaneously breathing group, subsequently returning to baseline values (see the supplementary materials at http://www.rcjournal.com). In the mechanically ventilated group, this change was observed at the end of exercise for subjects performing passive leg cycling. Systolic blood pressure was modified in the spontaneously breathing group but diastolic blood pressure was not. These heart rate or systolic blood pressure changes were not clinically relevant.

Subject Perception of Exercise

Overall, 22 subjects in the spontaneously breathing group and 9 in the mechanically ventilated group were able to provide ratings on the scales for pain, exertion, and enjoyment. Only the spontaneously breathing group presented an increase in self-perception of exertion. No changes were perceived in pain before and after exercise. Enjoyment after exercise was quite high in both groups (see the supplementary materials at http://www.rcjournal.com).

Discussion

The results of this study demonstrate that the association of a sitting position with physical activity significantly increases global EELI in critically ill subjects. In spontaneously breathing subjects, this improvement was evidenced in the posterior lung regions, whereas in mechanically ventilated subjects the increase was observed in the anterior zones. These recruitment-associated changes correlated with an improvement in P_{aO_2}/F_{IO_2} after the end of exercise. Both changes in EELI and oxygenation were more pronounced in subjects with a lower P_{aO_2}/F_{IO_2} at baseline.

Position changes and physical activity both improve respiratory physiology. Indeed, an upright position improves end-expiratory lung volume and oxygenation in mechanically ventilated subjects.[12,13,28] Furthermore, sitting and standing during the first day after major abdominal surgery increase arterial oxygen saturation,[16] and early ambulation associated with other physical therapy techniques (eg, incentive spirometry and positive expiratory airway pressure) prevents postoperative atelectasis.[17] In the same population, ambulation alone can prevent postoperative pulmonary complications, without the addition of respiratory exercises.[29] In this study, we have shown that seating subjects in a chair and having them perform different exercises was effective in improving lung aeration and oxygenation 20 min after exercise in both spontaneously breathing subjects and subjects on mechanical ventilation.

The mechanisms involved in the lung aeration and oxygenation improvements are not clear. Nevertheless, we hypothesize that an effective redistribution of air volume induced by the trunk's upright position, followed by exercise, could prevent respiratory monotony while in the resting state.[30] In patients on mechanical ventilation and those receiving high-flow oxygen therapy, in addition to the potential benefits that position change and gravity can induce in lung aeration, positive pressure can also improve the air volume redistribution. Other possible mechanisms are enhanced diaphragm utilization and an increase in transpulmonary pressure, especially during exercise. Moreover, because increased tidal impedance variation was observed in the posterior lung regions during active exercise without P_{aCO_2} changes, we suggest that oxygenation improvement is not explained by marked increases in minute ventilation.

Bedrest induces heterogeneity of ventilation, especially in posterior lung regions,[6] and is usually prevented by modifying PEEP levels and realizing position changes.[31] In this study, the objective was to demonstrate that subject mobilization without changes in PEEP would induce ventilation redistribution. In the mechanically ventilated group, EELI changes were more pronounced in the anterior lung regions compared to spontaneously breathing subjects, in whom the posterior lung regions benefited more. However, the homogeneity index[24] was not modified in any group after intervention, with the exception of the spontaneously breathing subjects performing leg cycling. This lack of effect in the subjects on mechanical ventilation is probably due to the homogeneity already present at baseline during pressure support ventilation, characterized by an enhanced utilization of the diaphragm compared with the controlled mechanical ventilation.[32]

An observational study of abdominal postoperative subjects on mechanical ventilation reported a momentary increase in minute ventilation during standing, without an increase in oxygenation.[15] In this report, we observed increased breathing frequency during exercise, especially active exercise, with a trend toward an increase in minute ventilation (only assessed in subjects on mechanical ventilation); however, the slight effort made by subjects (ie, $\sim$ 3 watts) could explain the results. Moreover, changes in P_{aO_2}/F_{IO_2} were more pronounced in subjects with $P_{aO_2}/F_{IO_2} < 200$, in parallel with EELI values, suggesting that the more severely hypoxemic subjects benefitted more from this intervention and that there is probably a higher recruitment potential. Similarly, mechanically ventilated subjects presented a positive correlation between P_{aO_2}/F_{IO_2} and the proportion of regional ventilation in the posterior lung regions, as reported previously after an increase in PEEP levels.[24]

Even if the oxygenation improvement is limited, it is essential to note that this kind of intervention was not detrimental to critically ill subjects, as it did not induce any adverse events, lactate increases, hypoxemic changes, or negative effects on lung aeration. Regarding the safety of spontaneous ventilation and potential increase in transpulmonary pressure in more severely ill patients, this seems not to be a problem in our population, as the inclusion period did not consider the first 48 h of mechanical ventilation.

Stiller et al[33] reported increases in heart rate and systolic and diastolic blood pressure associated with sitting, standing, and walking. The active use of a cycle ergometer for 5 min by subjects in the ICU caused a slight increase in the sensation of dyspnea, from mild to moderate, and was associated with increases in heart and breathing frequency.[34] In our study, active pedaling for 15 min increased dyspnea in the spontaneously breathing group and caused an acute increase in breathing frequency and heart rate. However, even if exercise is considered an exertion, the self-perception ratings showed that it was enjoyed by the subjects.

Study Limitations

This was a single-center study and may lack external validity. Because the EIT measurement is based on a lung slice, even though no change in the belt position was detected and variation in EIT value induced by different body positions is minimal in a healthy population,[35] we cannot be certain that the lung zone analyzed was modified by the body position change and the effects that gravity could have on pulmonary tissue or intrapulmonary liquids draining in patients with pulmonary illness. The population was highly heterogeneous and the spontaneously breathing subjects were not highly hypoxemic, thus a ceiling effect cannot be excluded. Similarly, the different activities proposed in our protocol could also be a limitation to the results' interpretation. Another possible source of bias is the utilization of high-flow oxygen therapy in 2 subjects from the spontaneously breathing group, in whom an effect related to the flow assistance induced by this therapy cannot be excluded. It is difficult to extrapolate our results to patients on controlled mechanical ventilation because all subjects were ventilated with spontaneous modes; this factor could also affect the baseline homogeneity of the ventilation distribution.[32] In our clinical practice, we were unable to calculate regional compliance or tidal volume using EIT software because we did not connect the EIT device to a ventilator produced by the same manufacturer, which limited our ability to detect changes in minute ventilation, especially in spontaneously breathing subjects. Another limitation of our study is the lack of additional measures to support our hypotheses, such as transpulmonary pressure on subjects on mechanical ventilation or diaphragm utilization. Nevertheless, the results of our study are novel and support further investigations.

Conclusions

These findings have essential implications for clinical practice and indicate that a sitting position coupled with early exercise was an effective method to increase lung aeration and oxygenation in critically ill subjects, especially in those with a lower baseline P_{aO_2}/F_{IO_2} and those performing active exercise.

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