TARGETED LATERAL POSITIONING DECREASES LUNG COLLAPSE AND OVERDISTENSION IN COVID-19-ASSOCIATED ARDS

Mikuláš Mlček M.D., Ph.D.[1†], Michal Otáhal M.D., Ph.D.[1,2†], João Batista Borges M.D., Ph.D.[*1], Glasiele Cristina Alcala P.T.[3], Dominik Hladík M.D.[1,2], Eduard Kuriščák M.D., Ph.D.[1], Leoš Tejkl[1], Marcelo Amato Prof., M.D., Ph.D.[3], Otomar Kittnar Prof., M.D., Ph.D.[1]

1 Institute of Physiology, First Faculty of Medicine, Charles University, Prague, Czech Republic

2 Department of Anaesthesiology, Resuscitation and Intensive Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, Czech Republic

3 Pulmonology Division, Cardiopulmonary Department, Heart Institute, University of Sao Paulo, São Paulo, Brazil

Corresponding author: João Batista Borges, M.D., Ph.D., Albertov 5, Prague, 128 00; e-mail: joaobatistaborges8@gmail.com

Sources of funding:

Technology Agency of the Czech Republic, FW 01010679

Progres 206-041

† Mikuláš Mlček and Michal Otáhal contributed equally to this work.

A majority of critically ill patients with coronavirus disease 2019 (caused by severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) (1) develops acute respiratory distress syndrome (ARDS), needs mechanical ventilation for prolonged time, and exhibits high mortality (2). In a large cohort study with 3988 critically ill patients with COVID-19 referred for intensive care unit (ICU) (2), positive end-expiratory pressure (PEEP) levels were higher than those reported for the management of moderate-to-severe ARDS in the pre–COVID-19 era; and, along with high fraction of inspired oxygen ($F_{I}O_2$) and low partial pressure of arterial oxygen ratio ($PaO_2/F_{I}O_2$) at ICU admission, were an independent factor associated with high mortality. Lung heterogeneity, hypoxemia disproportional to mechanics, right-left lung aeration asymmetry (3), and poorly recruitable lungs with increased recruitability with alternating body position between supine and prone (4) have been reported. However, real-time effects of changing body position and PEEP on regional overdistension and collapse, in individual patients, remain largely unknown and not timely monitored.

Lung collapse usually predominates within the most dependent units where the transpulmonary pressure (P_L = airways pressure − pleural pressure) is the lowest, while lung overdistension predominates within the most nondependent ones where the P_L is the highest. When there is right-left lung heterogeneity of collapse and overdistension, as in many patients with COVID-19 ARDS, a targeted lateral positioning strategy is conceivable: by one-sided lateral position, the lung with more collapsed units in supine position can be positioned gravity-nondependent (mostly) and, conversely, the lung with more overdistended units in supine position can be positioned gravity-dependent. Such targeted lateral position, by which P_L becomes larger in the nondependent units and smaller in the dependent ones, may afford simultaneous regional/selective recruitment and relief of overdistension effects.

Methods

We use electrical impedance tomography (EIT) with decremental PEEP titration algorithm ($PEEP_{EIT\text{-}titration}$) (5), which provides information on regional overdistension and collapse, to individualize PEEP and body position aiming to minimize ventilator-induced lung injury (VILI) mechanisms, namely collapse and overdistension.

Sixteen $PEEP_{EIT\text{-}titration}$ were performed in the first days of mechanical ventilation in five consecutive patients with COVID-19 ARDS (8 pairs supine vs. targeted lateral position): supine position immediately followed by the corresponding 30° targeted lateral position. The choice of lateral tilt was based on X-Ray: the less aerated lung was positioned up.

The same lung recruitment maneuver was performed before all $PEEP_{EIT\text{-}titration}$. $PEEP_{EIT\text{-}titration}$ consisted of decremental PEEP steps until reaching a PEEP level set by the clinician.

All $PEEP_{EIT\text{-}titration}$ were analyzed to quantify the amounts of collapse and overdistension, for each lung, at each PEEP step.

Results

All patients exhibited less aeration and ventilation in the left lung, thus the right (down) lateral tilt was decided.

Collapse-Left Lung: There was a statistically significant two-way interaction between position (supine vs. targeted lateral) and PEEP (P=0.014; two-way repeated measures ANOVA) in the % of collapse within the left lung: less collapse along the PEEP titration was found within the left lung in targeted lateral than supine position (Figure 1). Additionally, when the simple main effects were tested, the following significant differences were found: PEEP 14 (*P*=0.034), PEEP 10 (*P*=0.028), PEEP 8 (*P*=0.019), and PEEP 6 (*P*=0.007).

Overdistension-Right Lung: There was a marginal two-way interaction between position and PEEP (*P*=0.073; two-way repeated measures ANOVA). The main effect of position showed a statistically significant difference in the % of overdistension within the right lung: less overdistension along the PEEP titration in targeted lateral (right down) than supine position (*P*=0.005; Figure 2). The main effect of PEEP on right lung overdistension showed a statistically significant difference (*P*<0.0005). Additionally, for many PEEP levels significant *P* values were found in the pairwise comparisons with adjustment for multiple comparisons (Bonferroni).

Collapse-Right Lung and Overdistension-Left Lung: No statistically significant differences were found for position.

Discussion

A major focus of mechanical ventilation for COVID-19 is the avoidance of VILI while facilitating gas exchange via lung-protective ventilation. This is the first description of using EIT with targeted lateral positioning to personalize PEEP in adult patients with COVID-19 ARDS. A randomized and controlled trial demonstrated the feasibility and efficacy of a postural recruitment maneuver in children with anesthesia-induced atelectasis (6). Besides being applied in children and healthy lungs, another difference in relation to our study is the lack of PEEP titrations.

The vertical gradient of P_L, which is mainly due to gravity, changes with body mass and posture (7). Agostoni and D'Angelo showed that the P_L gradient increased when body position was changed from supine to lateral position (8). They demonstrated that lateral position leads to higher P_L in the most nondependent units and lower P_L in the most dependent ones. That is mainly because the thoracic right-to-left distance is longer than the anterior–posterior. Thus, generally, lateral positioning increases heterogeneity of P_L across the parenchyma, but this depends on PEEP and baseline lung conditions: recent reports in children have shown that an optimized PEEP after lateralization can minimize hyperdistension (maximizing ventilation) in a nondependent, sicker lung, while reasonably keeping functional residual capacity in dependent, healthier lung (9). Our $PEEP_{EIT\text{-}titration}$ seems to be a promising tool to find such personalized PEEP at the bedside.

Another potential beneficial effect of the targeted lateral positioning is an improved ventilation/perfusion matching due to: 1) attenuation of regional overdistension within the more aerated lung and, consequently, less diversion of pulmonary blood flow away from these units; 2) diminution of regional collapse within the less aerated lung. The consequent improvement of oxygenation may be important in these patients to manage their disproportional hypoxemia and “buy time” with minimum additional damage.

Our findings suggest the importance of timely PEEP titrations, tackling the dynamically changing phases of this disease. They suggest the relevance of personalized PEEP adjustments every time body positions are changed. The recommendation of applying nonpersonalized low or high PEEP may lead to insufficient and/or excessive PEEP in terms of protection of VILI (10).

In conclusion, targeted lateral positioning with bedside personalized PEEP provided a selective attenuation of overdistension and collapse in mechanically ventilated patients with COVID-19 ARDS and right-left lung aeration asymmetry.

References

1. Coronaviridae Study Group of the International Committee on Taxonomy of V. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nature microbiology* 2020; 5: 536-544.

2. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, Cattaneo S, Cereda D, Colombo S, Coluccello A, Crescini G, Forastieri Molinari A, Foti G, Fumagalli R, Iotti GA, Langer T, Latronico N, Lorini FL, Mojoli F, Natalini G, Pessina CM, Ranieri VM, Rech R, Scudeller L, Rosano A, Storti E, Thompson BT, Tirani M, Villani PG, Pesenti A, Cecconi M, Network C-LI. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA internal medicine* 2020.

3. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, Greninger AL, Pipavath S, Wurfel MM, Evans L, Kritek PA, West TE, Luks A, Gerbino A, Dale CR, Goldman JD, O'Mahony S, Mikacenic C. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med* 2020; 382: 2012-2022.

4. Pan C, Chen L, Lu C, Zhang W, Xia JA, Sklar MC, Du B, Brochard L, Qiu H. Lung Recruitability in COVID-19-associated Acute Respiratory Distress Syndrome: A Single-Center Observational Study. *Am J Respir Crit Care Med* 2020; 201: 1294-1297.

5. Costa EL, Borges JB, Melo A, Suarez-Sipmann F, Toufen C, Jr., Bohm SH, Amato MB. Bedside estimation of recruitable alveolar collapse and hyperdistension by electrical impedance tomography. *Intensive Care Med* 2009; 35: 1132-1137.

6. Acosta CM, Volpicelli G, Rudzik N, Venturin N, Gerez S, Ricci L, Natal M, Tusman G. Feasibility of postural lung recruitment maneuver in children: a randomized, controlled study. *The ultrasound journal* 2020; 12: 34.

7. D'Angelo E, Bonanni MV, Michelini S, Agostoni E. Topography of the pleural pressure in rabbits and dogs. *Respir Physiol* 1970; 8: 204-229.

8. Agostoni E, D'Angelo E, Bonanni MV. The effect of the abdomen on the vertical gradient of pleural surface pressure. *Respir Physiol* 1970; 8: 332-346.

9. Schibler A, Henning R. Positive end-expiratory pressure and ventilation inhomogeneity in mechanically ventilated children. *Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies* 2002; 3: 124-128.

10. Fan E, Beitler JR, Brochard L, Calfee CS, Ferguson ND, Slutsky AS, Brodie D. COVID-19-associated acute respiratory distress syndrome: is a different approach to management warranted? *Lancet Respir Med* 2020; 8: 816-821.

FIGURE LEGENDS

Figure 1: Lung collapse and overdistension by electrical impedance tomography in supine vs. targeted lateral body position within the left lung.

Left-to-right lung asymmetry was present on initial X-Ray taken in supine body position: unequivocally more opacities within the left lung. Thus lateral right positioning (30°) was indicated ("targeted") and performed with the platform-based rotation bed Multicare® (LINET). Line graphs of electrical impedance tomography (EIT)-based estimations of collapse and overdistension during decremental positive end-expiratory pressure (PEEP) titrations (supine vs. targeted lateral body position) are shown (mean ± SEM). Some illustrative and representative EIT images of collapse are also shown: collapsed pixels in purple. Note that the amount of collapsed units within the left lung in the supine body position was minimized in the lateral right one.

X axis: Decremental PEEP levels of the EIT-PEEP titrations.

Y axis: Percent of overdistended and collapsed lung units out of the total lung imaged by EIT.

Triangle: Supine body position.

Square: Targeted lateral body position (lateral right).

Black triangle and black square: Percent of collapsed lung units out of the total lung imaged by EIT.

White triangle and white semi-filled square: Percent of overdistended lung units out of the total lung imaged by EIT.

Figure 2: Lung collapse and overdistension by electrical impedance tomography in supine vs. targeted lateral body position within the right lung.

Left-to-right lung asymmetry was present on initial X-Ray taken in supine body position: unequivocally more opacities within the left lung. Thus lateral right positioning (30°) was indicated ("targeted") and performed with the platform-based rotation bed Multicare® (LINET). Line graphs of electrical impedance tomography (EIT)-based estimations of collapse and overdistension during decremental positive end-expiratory pressure (PEEP) titrations (supine vs. targeted lateral body position) are shown (mean ± SEM). Some illustrative and representative EIT images of overdistension are also shown: overdistended pixels in white. Note the asymmetric distribution of overdistension between the right and left lungs (concentration and predominance of overdistension within the right lung); and that the amount of overdistended units within the right lung in the supine body position was minimized in the lateral right one. Also note that the regional distribution of overdistension in the supine body position was much less gravitational-dependent than it is usually present in "typical" acute respiratory distress syndrome.

X axis: Decremental PEEP levels of the EIT-PEEP titrations.

Y axis: Percent of overdistended and collapsed lung units out of the total lung imaged by EIT.

Triangle: Supine body position.

Square: Targeted lateral body position (lateral right).

Black triangle and black square: Percent of collapsed lung units out of the total lung imaged by EIT.

White triangle and white semi-filled square: Percent of overdistended lung units out of the total lung imaged by EIT.

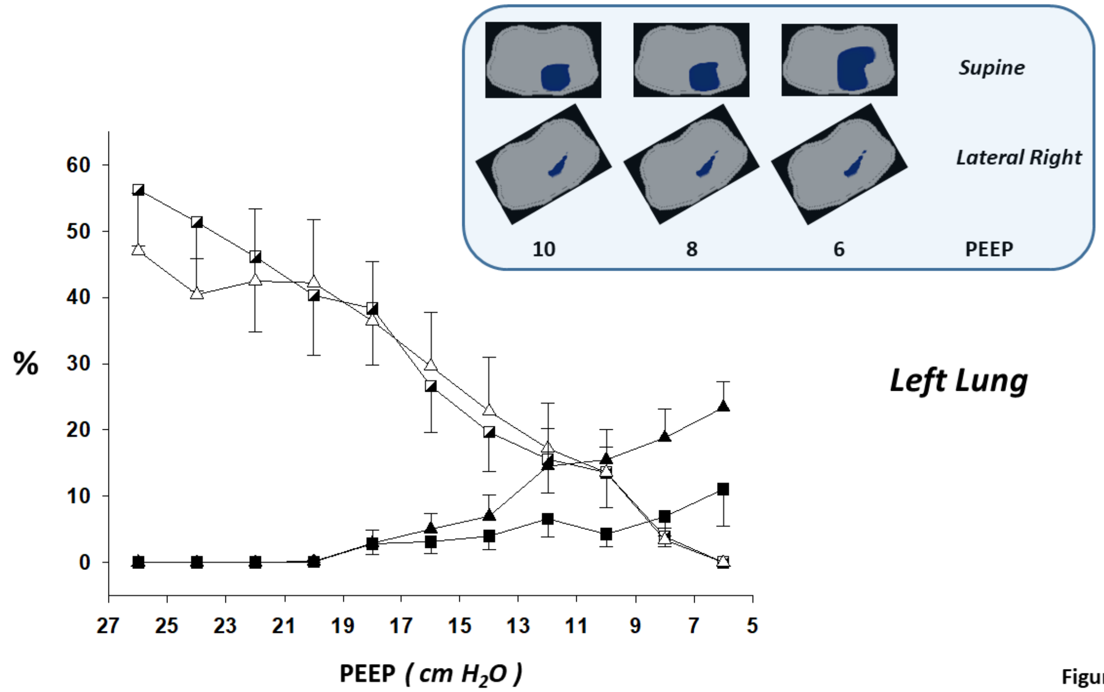

Figure 1

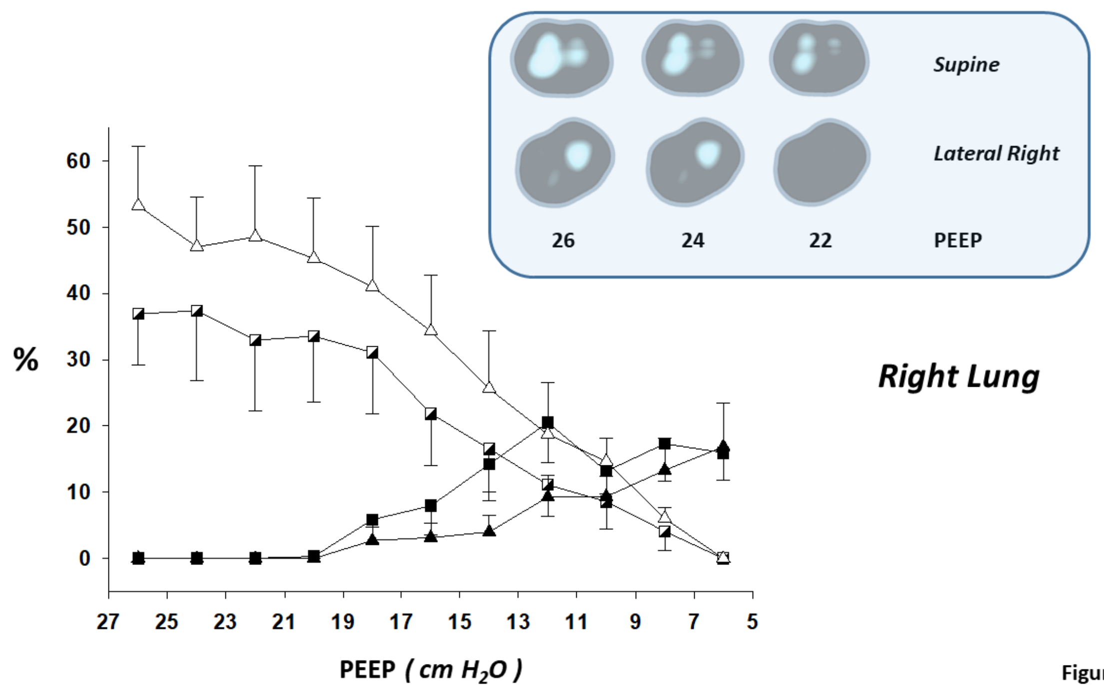

Figure 2