Effects of prone position on lung recruitment and ventilation-perfusion matching in patients with COVID-19 acute respiratory distress syndrome.

A combined CT-scan/Electrical Impedance Tomography study

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Online supplement

**Methods**

*Gas exchange data computation*

Partial alveolar pressure of O2 (PAO2) was calculated by the simplified Riley and Cournand equation: [FiO2 \* (PB-PH2O)] – (PaCO2/RER) [E1]. We assumed standard values for barometric pressure (PB) and partial pressure of H2O (PH2O) and respiratory exchange ratio (RER) of 760 torr, 47 torr and 0.8, respectively. PaCO2 is the measured arterial partial pressure of CO2. Alveolo-arterial difference in O2 (D(A-a)O2) was obtained as PAO2 minus arterial pressure in O2 (PaO2). Venous admixture (QVA/QT) was calculated as previously described by using central venous and arterial blood gas analyses [E2]. Corrected minute ventilation (VMcorr) was computed as (minute ventilation \* PaCO2)/40, and Ventilatory Ratio (VR) as (minute ventilation \* PaCO2)/(PBW\*37.5\*100) [E3].

*Respiratory mechanics data computation*

Respiratory mechanics were measured by tele-inspiratory and tele-expiratory occlusions of 2-3 seconds. Driving pressure was measured as plateau pressure (Pplat) minus total PEEP (PEEPtot). Respiratory system compliance (CRS) was calculated as the ratio between tidal volume and driving pressure and standardized respiratory system elastance (ERS) as the ratio between driving pressure and tidal volume per kilograms of PBW [E4].

*CT-scan analysis*

CT-scans were performed by an experienced team, using a 64-MDCT Lightspeed system (GE Medical Systems, Milwaukee, WI, USA). All CT-scan acquisitions were centralized, manually contoured by 2 independent researchers and analyzed offline, using standard software (Maluna v3.7, Mannheim, Germany).

Quantitative analysis allowed computation of global lung weight, and the proportions of hyperinflated, normally-, poorly- and non-aerated lung weight, as previously described [E5]. This analysis was performed also at the regional level for ventral and dorsal lung, by splitting each CT slices in two equal regions of interest.

Recruitment (or de-recruitment) between supine and prone position at global and regional level was computed as the decrease (or increase, respectively) in non-aerated weight, divided by the global lung weight in the supine position [E5].

Lung gas volume was measured at the global and regional levels, as previously described [E5]. We also computed the mean Hounsfield Units (HU) intensity, defined by the sum of HU\*density (for each HU range), divided by the total density. This mean number was calculated both for ventral and dorsal regions, and for each CT compartment (total, hyperinflated, normally, poorly and non-aerated) [E6].

*EIT data management and computation*

EIT data were stored for offline analysis performed at the global and regional level, by splitting the EIT functional image in 2 same-size ventral and dorsal regions of interest [E7]. Regional distribution of ventilation was measured as previously described.

To assess ventilation-perfusion matching, the pulmonary perfusion map was obtained from the slope of the impedance deflection following a 10 ml bolus of a NaCl 5% solution injected during a tele-inspiratory occlusion, after the removal of the heart and large vessels components [E8]. A filter of 10% of the maximal impedance variation was then applied for recognition of ventilated and/or perfused pixels. Overlap of these two images allowed the detection of ventilated and non-perfused units (only ventilated, indicating dead space) and vice versa (only perfused, indicating shunt). The ratio between these two measures was computed as the dead-space/shunt ratio [E9].

*Time-impedance curve concavity index*

The authors measured a time-impedance curve concavity index, based on a similar concept than the stress index [E9]. The slope of the global and regional time-impedance curves was fitted with a power equation y = a\*Δtb + c, as previously described [E10]. We assumed that, everything being equal in a mode with constant pressure, this curve was an acceptable surrogate for the pressure-volume curve (Figure E1), and we hypothesized that higher “b coefficient” (i.e., more pronounced concavity of the time-impedance curve during insufflation) may indicate larger amount of units opening during inspiration leading to higher risk of atelectrauma (Figure E1).

**References**

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# Additional Table

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Supine****n = 21** | **Prone****n = 21** | **p value** |
|  |  |  |  |
| **CT-scan global analysis** |  |  |  |
| Total lung weight, g | 1466 (±378) | 1394 (±381) | **.007** |
| Hyperinflated lung weight, g | 14 (±12) | 12 (±9) | **.008** |
| Normally aerated lung weight, g | 356 (±132) | 400 (±164)  | **.004** |
| Poorly aerated lung weight, g | 525 (±192) | 505 (±173)  | .335 |
| Non-aerated lung weight, g | 571 (±294) | 477 (±249)  | **.001** |
| Lung volume, mL | 1402 (±599) | 1462 (±612)  | .117 |
|  |  |  |  |
| **CT-scan ventral regions analysis**  |  |  |  |
| Total lung weight, g | 531 (±133) | 632 (±189) | **<.001** |
| Hyperinflated lung weight, g | 10 (±9) | 4 (±4) | **<.001** |
| Normally aerated lung weight, g | 187 (±69) | 148 (±66) | **<.001** |
| Poorly aerated lung weight, g | 183 (±74) | 222 (±93) | **.019** |
| Non-aerated lung weight, g | 152 (±84) | 257 (±140) | **<.001** |
| Lung volume, mL | 785 (±351) | 541 (±265) | **<.001** |
|  |  |  |  |
| **CT-scan dorsal regions analysis** |  |  |  |
| Total lung weight, g | 965 (±264) | 803 (±252) | **<.001** |
| Hyperinflated lung weight, g | 4 (±4) | 8 (±6) | **<.001** |
| Normally aerated lung weight, g | 177 (±75) | 260 (±115) | **<.001** |
| Poorly aerated lung weight, g | 353 (±142) | 295 (±118) | **.015** |
| Non-aerated lung weight, g | 431 (±238) | 239 (±149) | **<.001** |
| Lung volume, mL | 641 (±271) | 930 (±350) | **<.001** |
|  |  |  |  |

**Table E1.** **Regional quantitative CT-scan analysis between the supine and prone positions.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Supine****n = 21** | **Prone****n = 21** | **p value** |
|  |  |  |  |
| **Ventral regions** |  |  |  |
| Mean HU global | -623 [-662 - -444] | -458 [-562 - -333] | <.001 |
| Mean HU hyperinflated | -939 [-941 - -939] | - 939 [-941 – 938] | .224 |
| Mean HU normally aerated | -729 [-770 - -705] | -707 [-735 - -685] | <.001 |
| Mean HU poorly aerated | -328 [-340 - -310] | -309 [-320 - -285] | <.001 |
| Mean HU non-aerated | 18 [11-27] | 11 [4-16] | <.001 |
|  |  |  |  |
| **Dorsal regions** |  |  |  |
| Mean HU global | -421 [-493 - -296] | -540 [-603 - -481] | <.001 |
| Mean HU hyperinflated | -940 [-941 - -939] | -940 [-941 - -938] | .426 |
| Mean HU normally aerated | -696 [-723 - -670] | -707 [-746 - -697] | <.001 |
| Mean HU poorly aerated | -304 [-319 - -282] | -332 [-347 - -317] | <.001 |
| Mean HU non-aerated | 16 [7-21] | 24 [17-31] | <.001 |
|  |  |  |  |

**Table E2. Mean CT numbers distribution, expressed in Hounsfield Units (HU), according to each CT-scan based lung compartment.**

# Additional Figures



**Figure E1. Determinants of the power equation to compute the time-impedance curve index for a given tidal breathe.** The inspiratory part of the curve is fitted with the following equation: z = a\*Δtb + c. a represents the slope of the curve, b its concavity (this is, the measured index), and c the baseline value at the beginning of the cycle. The higher b is, the more concave the curve is, which could be related to atelectrauma.

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**Figure E2. Distribution of the global weight among lung components between supine (orange bars) and prone (blue bars) position.** \*p<0.05



**Figure E3. Variation of the amount of only ventilated (blue boxes) and only perfused (red boxes) lung units between the supine and prone positions.** \*p<0.05, box plots in Tukey representation.



**Figure E4. Individual values and box plots (mean with Tukey representation) of respiratory system compliance (A, CRS), PaO2/FiO2 ratio (B) and PaCO2 (C).** \*p<0.05



**Figure E5. Association between global and regional (de)recruitment, and change in PaO2/FiO2 ratio.** Note the absence of correlation (rho=0.091, p=0.703 for the global lungs; rho=0.317, p=0.173 for the ventral regions, and rho=0.184, p=0.436 for the dorsal ones).



**Figure E6. Effect of prone positioning on recruitment among subgroups, in global and regional lung regions**. ERS: respiratory system elastance.