**External Chest-Wall Compression in COVID-19 ARDS with Low-Compliance: a Physiological Study.**

L. Bastia1, E. Rezoagli2,3, M. Guarnieri4, D. Engelberts5, C. Forlini4, F. Marrazzo4, S. Spina4, G. Bassi4, R. Giudici4, M. Post5, G. Bellani2,3, R. Fumagalli2,4, L. J. Brochard6\*, T. Langer2,4\*

**ONLINE SUPPLEMENT**

**FIGURE LEGENDS**

**Figure E1. Study protocol.** Protocol made of 4 steps (4 squares in the picture), PEEP was kept constant for the first 3 steps and then reduced for the last step. ECC: external chest-wall compression. + = brief ECC during an end-expiratory hold maneuver,\*= static respiratory mechanics measurements, § = arterial and venous blood gas samples collection.

**Figure E2. Brief chest compression during baseline.** In order to detect the pressure applied to respiratory system from a 5 lt saline bag above the thorax we performed this brief maneuver during an expiratory pause. 1) Pressure wave-form of a volume-controlled ventilation modality; 2) expiratory hold starts; 3) application of 5 lt saline bag; 4) increased airway pressure caused by the 5 lt saline bag detected by the ventilator; 5) 5 lt saline bag removed. Paw = airway pressure.

**Figure E3. Delta end-expiratory transpulmonary pressure (PLexp) and delta end-inspiratory transpulmonary pressure (PLinsp) compared to baseline.** N = 9,Panel A shows the change in PLexp for each time-point compared to baseline (gray dashed line), no significant differences were found although the ECC led to a decrease of PLexp. Panel B shows the change in PLinsp for each time-point compared to baseline (gray dashed line). ECC reduced significantly PLinsp, as for driving pressure the ECC effect on PLinsp in influenced by time. ECC: external chest-wall compression. \* = P < 0.05 of absolute values of different timepoints versus baseline.

**Figure E4. Tidal Volume (Vt) Distribution.** N = 11. Panel A, Vt distribution expressed in % across steps: ventilation is predominantly non-dependent (white dots) and is fairly stable during the protocol. Panel B, Vt distribution expressed in delta % from baseline: ECC led to significant increase in the non-dependent ventilation after 5 minutes and after PEEP reduction. However, this difference compared to baseline is lost at 30 and 60 min of ECC. ECC: external chest-wall compression. \* = P < 0.05 of absolute values of different timepoints versus baseline.

**Figure E5. Change in Non-Dependent Tidal Volume (Vt) produced by ECC VS change in Non-Dependent Vt produced by PEEP reduction, expressed in % compared to Baseline.** N = 11.Relationship between non-dependent Vt variations obtained after 5 minutes of ECC (5 min ECC non-dependent Vt % – baseline non-dependent Vt%) and non-dependent Vt variations obtained after PEEP reduction (PEEP reduction non-dependent Vt % – baseline non-dependent Vt%). A linear relationship in the degree of Vt change produced by ECC and PEEP reduction was observed (R = 0.72, R2 = 0.51, P = 0.01). Suggesting that ECC and PEEP reduction generates similar redistribution in regional ventilation. ECC: external chest-wall compression.

**Figure E6. Representative behavior of end-expiratory lung impedance (EELI) before and after an ECC.** From to bottom EELI of global lung, region of interest (ROI) 1, ROI 2, ROI 3 and ROI 4. Black dashed line: ECC start, red solid line: EELI baseline, red dashed line: EELI right after ECC. Importantly to underline that 1) EELI is reducing over time globally and 2) EELI is reducing mainly in ROI 2. ECC: external chest-wall compression.

**Figure E7. Delta end-expiratory lung impedance (EELI) during ECC.** N = 11. The sustained ECC led to a decrease of ELLI (a surrogate of end-expiratory lung volume) in the non-dependent lung (white dots) reaching statistical significance after 60 minutes compared to the onset of ECC placement (i.e. 5 minutes). The EELI in the dependent lung (black dots) did not change over time.ECC: external chest-wall compression. \* = P < 0.05 of differences between the absolute values of timepoints at 30 and 60 minutes versus 5 minutes.

**Figure E8. Bland-Altmann Plot, difference in driving pressure decrease between ECC and PEEP reduction.** The graph shows a good agreement between the two procedures. Bias = -0.86, upper limit of agreement = 0.40, lower limit of agreement = -2.13. DP: driving pressure, ECC: external chest-wall compression. DP: driving pressure, LOA: limit of agreement.

**Figure E9. Spaghetti plot of Driving Pressure across study steps.** Every line represents a single patient throughout the protocol. ECC: external chest-wall compression.

**Figure E10. Spaghetti plot of Lung compliance (A) and chest-wall compliance (B) across study steps.** Every line represents a single patient throughout the protocol. To note, patients #9 and #11 are not reported because of the absence of esophageal balloon. ECC: external chest-wall compression.

**Figure E11. Spaghetti plot of Dorsal Fraction of Ventilation across study steps.** Every line represents a single patient throughout the protocol. This graph represents the percentage of ventilation received from the dorsal part of the lung (*i.e.*, dependent). Grey dashed line = 50% = equal distribution between dorsal and ventral. 0% means no ventilation in the dorsal lung. ECC: external chest-wall compression.

**Figure E12. Spaghetti plot of Non-dependent (A) and Dependent (B) regional Crs across study steps.** Every line represents a single patient throughout the protocol. ECC: external chest-wall compression. Crs: respiratory system compliance.

**Figure E13. Respiratory System Pressure-Volume (PV) curve at baseline and after a quick external chest compression (ECC), possible mechanism.** PV-curve baseline (light blue solid curve) is shifted downward from ECC (light blue dashed line) because of the end-expiratory volume reduction (Y axes). PEEP (black dots) does not change however, for the same amount of tidal volume (VT), plateau pressure (Pplat) at baseline is higher compared to Pplat after ECC (red dots). This change in Pplat implies a change in driving pressure (DP) on the X axes with lower DP associated with ECC.

**TABLES**

**Table E1. Esophageal balloon positioning**

|  |  |
| --- | --- |
|  |  |
| Distance from nose to balloon of the esophageal catheter (cm) | 39 ± 3 |
| ΔPes/ΔPaw | 1.01 ± 0.15 |

Data are expressed as mean ± standard deviation. ΔPes: variation of esophageal pressure caused by a chest compression performed during an end-expiratory hold. ΔPaw: variation of airway pressure caused by a chest compression performed during an end-expiratory hold.

**Table E2. Respiratory Mechanics Variables Through Steps**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | ECC 5 min | ECC 30 min | ECC 60 min | ECC Disc | PEEP Reduction |
| DP(cmH2O) | 14.2 ± 1.3 | 12.3 ± 1.3\*-11.7%(-21.6 – -8.2%) | 12.7 ± 1.4\*-7.7%(-16.2 – -3.5%) | 13.3 ± 1.5\*-4.8%(-12.4 – +2.8%) | 14.9 ± 1.8+0.7%(-0.1% – +10.0%) | 13.1 ± 1.3\*-6.2%(-15.8 – 0.0%) |
| PEEPt | 12.6 ± 2.9 | 12.8 ± 2.9 | 12.6 ± 2.9 | 12.6 ± 3 | 12.6 ± 3 | 9.8 ± 2.9\* |
| Pplat(cmH2O) | 27(26 – 28.2) | 24.6(22.8 – 27.7)-5.7%(-8.8 – -4.2%) | 25(22.8 – 28)-5.0%(-8.8 – -0.7%) | 25.7(23 – 29)-3.7%(-7.1 – 2.8%) | 28.4(26.4 – 29)+0.7%(0.0 – +5.9%) | 22.5\*(20 – 24.8)-13.5%(-18.5 – -12.1%) |
| Crs(mL/cmH2O) | 25.9 ± 5.9 | 30.2 ± 7.8\*+16.3 ± 11.7% | 29.2 ± 7.7\*+12.2% ± 10.3 | 28.0 ± 7.7+7.4 ± 11.8% | 24.9 ± 6.3-4.3 ± 6.8% | 28.3 ± 7.8\*+8.8 ± 12.6% |
| ELrs(cmH2O/mL) | 37[34 – 45] | 31\*[28 – 41] | 33[29 – 41] | 34[32 – 44] | 40#[35 – 45] | 33[32 – 45] |
| Ccw(mL/cmH2O) | 152(120.2 – 305.1) | 172.7(108.7 – 295.2)-4.0%(-9.8% – +7.5%) | 153.8(109.6 – 348.9)-7.6%(-16.2 – +30.6%) | 160(96.3 – 326.7)-13.3%(-24.0 – +10.0%) | 187.5(151.5 – 312.8)+11.1%(-6.0 – +34.5%) | 327.3(151.5 – 401.1)+18.2%(+4.5 – +102.2%) |
| ELcw(cmH2O/mL) | 6 ± 2 | 6 ± 3 | 6 ± 3 | 6 ± 3 | 5 ± 1 | 4 ± 2 |
| Clung(mL/cmH2O) | 28.7 ± 6.1 | 35.5 ± 9.3\*+23.4 ± 14.9% | 33.3 ± 8\*+15.9 ± 11.3% | 32.1 ± 7.9+12.0 ± 16.2% | 26.5 ± 6.3§-7.5 ± 9.2% | 30.3 ± 6.3+6.3 ± 10.6% |
| ELlung(cmH2O/mL) | 33[29 – 42] | 27\*[22 – 37] | 28\*[24 – 38] | 30[25 – 42] | 39#[32 – 44] | 31[29 – 39] |
| MAP(cmH2O) | 17(15 – 20) | 17(15 – 20) | 17(15 – 20) | 17(15 – 20) | 17(15 – 21) | 14\*(12 – 17) |
| Non-Dependent Regional Crs(mL/cmH2O) | 16.4 ± 5.6 | 19.8 ± 6.6\*+16.9%(+14.3 – +33.7%) | 18.9 ± 6.7\*+14.1%(+9.4 – +19.3%) | 17.9 ± 6.5\*+11.8%(+1.0 – +18.8%) | 15.7 ± 5.1-2.7%(-7.4 – -0.01%) | 18.4 ± 6.1\*+15.4%(+2.8 – +23.6%) |
| DependentRegional Crs(mL/cmH2O) | 9.4 ± 2.2 | 10.3 ± 2.8+5.8 ± 9.5%  | 10.2 ± 2.7+3.9 ± 10.6% | 9.9 ± 2.5+2.2 ± 8.6% | 9 ± 2.5-5.1 ± 8.9% | 9.7 ± 3.1+2.5 ± 15.8% |
| End-Expiratory PL(cmH2O) | -1.7(-4.8 – 0.25) | -3.1(-5.6 – -1.5)-135.3%(-313.3 – -21.6%) | -3.5(-5.7 – -1.4)-109.1%(-344.6 – -35.9%) | -3(-5.6 – -0.5)-72.7%(-148.5 – -38.4%) | -0.4(-2 – 1.7)+36.4%(+2.3 – +124.5%) | -2.5(-4.4 – 0.7)-55.2%(-182.6 – +8.5%) |
| End-Inspiratory PL(cmH2O) | 11.7 ± 4.3 | 7.7 ± 5\*-38.9 ± 18.4% | 8.1 ± 5.2\*-34.9 ± 17.7% | 9.1 ± 5.1\*-25.3 ± 19.1% | 13.9 ± 4.3+21.4 ± 16.2% | 10 ± 4.4-15.3 ± 18.0% |

Data are expressed as median and interquartile range or mean ± standard deviation as appropriate. Percentages are expressed compared to baseline.ECC: external chest-wall compression, DP: driving pressure, Pplat: plateau pressure, Crs: respiratory system compliance, ELrs: respiratory system elastance, Ccw: chest-wall compliance, ELcw: chest-wall elastance, Clung: lung compliance, ELlung: lung elastance, MAP: mean airway pressure, PL: transpulmonary pressure. \*: P < 0.05 compared to baseline. § = P < 0.05 compared to ECC at 5, 30 and 60 minutes. # = P < 0.05 compared to ECC at 30 and 60 minutes.

**Table E3. Gas Exchange over time**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Baseline | ECC 60 min | ECC Discontinuation | PEEP Reduction | P-value |
| PaO2 (mmHg) | 88.2(77.1 – 127.6) | 71.6(66.2 – 85.4)-7.3%(-20.1 – +1.1%) | 84.9(68.1 – 134.8)-0.4%(-8.1 – +4.3%) | 85.7(66.8 – 129.5)-0.6%(-14.7 – +13.2%) | 0.20 |
| PaCO2 (mmHg) | 55.9 ± 6.6 | 53.5 ± 6.9-6.0%(-8.5 – +0.4%) | 53.1 ± 6.7-5.1%(-10.6 – +1.1%) | 52.2 ±8.2-3.9%(-10.0 – +0.6%) | 0.06 |
| pH | 7.371 ± 0.03 | 7.392 ± 0.03 | 7.386 ± 0.03 | 7.397 ± 0.03**\*** | 0.01 |
| PaO2/FiO2 | 163(109 – 220) | 136(109 – 200) | 150(113 – 202) | 162(110 – 227) | 0.20 |
| FiO2 (%) | 60(50 - 65) | 60(50 - 65) | 60(50 - 65) | 60(50 - 65) | 1.00 |
| End-tidal CO2 (mmHg) | 42(39 – 50) | 42(37 – 45) | 42(39- 49) | 41(37 – 46) | 0.08 |
| Dead space (%) | 18.6(12.6 – 27.1) | 20(14.7 – 26.7) | 14.7(7.5 – 24) | 18(11.4 – 26.9) | 0.24 |
| Ventilatory Ratio | 2.1 ± 0.4 | 2.07 ± 0.5 | 2.08 ± 0.4 | 2.02 ± 0.5 | 0.21 |
| Shunt fraction (%) | 15.5(7.1 – 27.3) | 19.0(7.0 – 25.0) | 18.9(7.1 – 27.0) | 15.0(9.6 – 25.6) | 0.69 |
| PAO2-PaO2 | 254.4(162.0 – 327.2) | 266.4**\***(164.1 – 328.7) | 253.7(163.1 – 321.4) | 245.1(149.6 – 327.8) | 0.02 |
| PAO2/PaO2 | 3.48(2.60 – 5.55) | 4.21(2.90 – 5.60) | 3.81(2.73 – 5.29) | 3.48(2.28 – 5.47) | 0.09 |

Data are expressed as median and interquartile range or mean ± standard deviation as appropriate. Percentages are expressed compared to baseline. ECC: external chest-wall compression. \*: P < 0.05 compared to baseline.

**Table E4. Hemodynamics over time**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | ECC 5 min | ECC 30 min | ECC 60 min | ECC Discon | PEEP Reduction | P-value |
| HR(bpm) | 93 ± 14 | 92 ± 13 | 91 ± 12 | 90 ± 11 | 93 ± 9 | 91 ± 14 | 0.50 |
| SAP (mmHg) | 126 ± 16 | 132 ± 19 | 135 ± 18 | 128 ± 12 | 128 ± 15 | 130 ± 17 | 0.30 |
| MAP (mmHg) | 79 ± 17 | 80 ± 13 | 84 ± 15 | 77 ± 12 | 77 ± 12 | 76 ± 16 | 0.10 |
| DAP (mmHg) | 67 ± 11 | 68 ± 5 | 70 ± 10 | 64 ± 12 | 66 ± 9 | 64 ± 11 | 0.40 |
| CVP (mmHg) | 9 ± 3 | 11 ± 3 | 10 ± 3 | 9 ± 3 | 9 ± 4 | 10 ± 3 | 0.06 |

Data are expressed as mean ± standard deviation as appropriate. ECC: external chest-wall compression, HR: heart rate, SAP: systolic arterial pressure, MAP: mean arterial pressure, DAP: diastolic arterial pressure, CVP: central venous pressure.