**The association of partial pressure of oxygen and carbon dioxide with neurological outcome after out-of-hospital cardiac arrest: an explorative International Cardiac Arrest Registry 2.0 study.**

ADDITIONAL FILE

Florian Ebner MD PhD, Richard R Riker MD, Zana HaxhijaMD, David B SederMD, Teresa L May DO MS, Susann UllénPhD, Pascal Stammet MD PhD, Karen HirschMD PhD, Sune ForsbergMD PhD, Allison Dupont MD, Hans Friberg MD PhD, John A McPhersonMD, Eldar Søreide MD PhD, Josef Dankiewicz MD PhD, Tobias Cronberg MD PhD, Niklas Nielsen MD PhD.

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| **Supplementary Table 1. Baseline characteristics of all patients and the PaO2 analysis groups** | | | | |
| **Demographic characteristic** | **All patients n = 2135** | **No-exposure n = 1133** | **Hyperoxemia n = 436** | **Hypoxemia n = 422** |
| Age in years, mean (SD) | 61.09 (15.9) | 61.52 (15.54) | 59.55 (16.41) | 61.18 (16.07) |
| Male sex, n (%) | 1432 (67.1) | 787 (69.5) | 269 (61.7) | 278 (65.9) |
| **Medical history** |  |  |  |  |
| Previous myocardial infarction n (%) | 370 (17.3) | 209 (18.4) | 71 (16.3) | 74 (17.5) |
| Chronic heart failure n (%) | 367 (17.2) | 186 (16.4) | 72 (16.5) | 77 (18.2) |
| COPD n (%) | 344 (16.1) | 168 (14.8) | 85 (19.5) | 78 (18.5) |
| Cerebro vascular disease n (%) | 196 (9.2) | 115 (10.2) | 32 (7.3) | 32 (7.6) |
| Diabetes mellitus n (%) | 521 (24.4) | 263 (23.2) | 104 (23.9) | 115 (27.3) |
| Obesity n (%) | 268 (15.3) | 133 (14.5) | 53 (14.2) | 67 (18.8) |
| **Cardiac arrest characteristic** |  |  |  |  |
| Witnessed cardiac arrest n (%) | 1591 (75.6) | 859 (76.9) | 315 (72.9) | 313 (74.9) |
| Bystander CPR n (%) | 1385 (65.5) | 749 (66.8) | 292 (67.1) | 261 (62.4) |
| Bystander defibrillation n (%) | 123 (5.8) | 72 (6.4) | 27 (6.2) | 17 (4.0) |
| Initial rhythm shockable n (%) | 1022 (50.0) | 597 (54.4) | 190 (46.1) | 179 (44.3) |
| Time to ROSC (min), median (IQR) | 29 (21 - 48) | 29 (21 – 48) | 29 (19 – 48) | 34 (24 – 48) |
| **Characteristic on arrival** |  |  |  |  |
| Sedated on arrival n (%) | 437 (21.7) | 236 (22.00) | 85 (20.1) | 80 (20.00) |
| GCS Motor 1 n (%) | 1544 (79.4) | 803 (77.7) | 325 (78.5) | 320 (82.9) |
| Circulatory shock on admission n (%) | 902 (44.2) | 447 (40.9) | 203 (47.5) | 203 (49.5) |
| Admission pH, median (IQR) | 7.20 (7.10 - 7.30) | 7.21 (7.10 – 7.30) | 7.21 (7.08 – 7.30) | 7.15 (7.02 – 7.25) |
| Admission lactate, mmol/l, median (IQR) | 6.4 (3.20 - 10.2) | 5.9 (2.80 – 9.50) | 7.20 (3.7 – 10.95) | 7.30 (3.90 – 11.20) |
| Bicarbonate on admission, mmol/l, median (IQR) | 18.0 (14.5 - 21.0) | 18.8 (15.0 – 21.0) | 17.55 (14.1 – 21.0) | 17.00 (13.93 – 21.0) |

n = number, SD = standard deviation, IQR = interquartile range, % = percent, mmol/l = millimole per liter, CPR = cardio pulmonary resuscitation, ROSC = return of spontaneous circulation, COPD = chronic obstructive pulmonary disease, GCS = Glasgow coma scale, PaO2 = arterial partial pressure of oxygen, all % are presented as valid percent.

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| **Supplementary Table 2. Baseline characteristics of all patients and the PaCO2 analysis groups** | | | | |
| **Demographic characteristic** | **All patients n = 2135** | **No-exposure n = 591** | **Hypercapnemia n = 896** | **Hypocapnemia n = 683** |
| Age in years, mean (SD) | 61.09 (15.9) | 60.85 (15.90) | 61.58 (15.18) | 59.55 (16.59) |
| Male sex, n (%) | 1432 (67.1) | 435 (73.6) | 589 (65.7) | 421 (61.6) |
| **Medical history** |  |  |  |  |
| Previous myocardial infarction n (%) | 370 (17.3) | 110 (18.6) | 164 (18.3) | 110 (16.1) |
| Chronic heart failure n (%) | 367 (17.2) | 105 (17.8) | 148 (16.5) | 115 (16.8) |
| COPD n (%) | 344 (16.1) | 60 (10.2) | 208 (23.2) | 67 (9.8) |
| Cerebro vascular disease n (%) | 196 (9.2) | 58 (9.8) | 76 (8.5) | 57 (8.3) |
| Diabetes mellitus n (%) | 521 (24.4) | 126 (21.3) | 223 (24.9) | 181 (26.5) |
| Obesity n (%) | 268 (15.3) | 63 (12.7) | 136 (18.9) | 84 (14.5) |
| **Cardiac arrest characteristic** |  |  |  |  |
| Witnessed cardiac arrest n (%) | 1591 (75.6) | 450 (77.2) | 659 (74.7) | 504 (74.6) |
| Bystander CPR n (%) | 1385 (65.5) | 390 (66.2) | 576 (64.9) | 449 (66.6) |
| Bystander defibrillation n (%) | 123 (5.8) | 42 (7.1) | 49 (5.5) | 34 (5.0) |
| Initial rhythm shockable n (%) | 1022 (50.0) | 321 (57.0) | 396 (45.3) | 340 (51.9) |
| Time to ROSC (min), median (IQR) | 29 (21.0 – 48.0) | 29 (19.0 – 47.50) | 29 (21.0 – 46.0) | 32 (21.0 – 48.0) |
| **Characteristic on arrival** |  |  |  |  |
| Sedated on arrival n (%) | 437 (21.7) | 131 (23.4) | 180 (20.9) | 134 (20.7) |
| GCS Motor 1 n (%) | 1544 (79.4) | 389 (72.2) | 689 (83.4) | 523 (82.4) |
| Circulatory shock on admission n (%) | 902 (44.2) | 231 (40.6) | 404 (46.4) | 315 (47.5) |
| Admission pH, median (IQR) | 7.20 (7.10 - 7.30) | 7.24 (7.15 – 7.32) | 7.15 (7.02 – 7.24) | 7.22 (7.10 – 7.31) |
| Admission lactate, mmol/l, median (IQR) | 6.4 (3.20 - 10.2) | 5.38 (2.8 – 9.5) | 7.07 (3.6 – 10.8) | 6.20 (3.1 – 10.4) |
| Bicarbonate on admission, mmol/l, median (IQR) | 18.0 (14.5 - 21.0) | 18.6 (15.0 – 21.0) | 18.8 (14.1 – 22.0) | 17.80 (14.0 – 20.1) |

n = number, SD = standard deviation, IQR = interquartile range, % = percent, mmol/l = millimole per liter, CPR = cardio pulmonary resuscitation, ROSC = return of spontaneous circulation, COPD = chronic obstructive pulmonary disease, GCS = Glasgow coma scale, PaCO2 = arterial partial pressure of carbon dioxide, all % are presented as valid percent.

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| **Supplementary Table 3. Sensitivity analysis. Association of exposure to extreme PaO2 and PaCO2 values with poor neurological outcome (Patients with extreme PaO2 or PaCO2 value double exposure removed)** | | | |
|  | **OR** | **95% CI** | **p-value** |
| Hyperoxemia versus PaO2 no-exposure | 1.44 | 0.97 - 2.14 | 0.07 |
| Hyperoxemia versus no-hyperoxemia | 1.37 | 0.94 - 2.02 | 0.11 |
| Hypoxemia versus PaO2 no-exposure | 1.36 | 0.91 - 2.03 | 0.13 |
| Hypoxemia versus no-hypoxemia | 1.26 | 0.86 - 1.86 | 0.24 |
| Hypercapnemia versus PaCO2 no-exposure | 0.83 | 0.58 - 1.18 | 0.29 |
| Hypercapnemia versus no-hypercapnemia | 0.82 | 0.59 - 1.12 | 0.21 |
| Hypocapnemia versus PaCO2 no-exposure | 1.30 | 0.88 - 1.93 | 0.19 |
| Hypocapnemia versus no-hypocapnemia | 1.25 | 0.89 - 1.77 | 0.20 |

OR = odds ratio, 95% CI = 95% confidence interval, PaO2= arterial partial pressure of oxygen, PaCO2= arterial partial pressure of carbon dioxide. Hyperoxemia = PaO2 >40 kPa, Hypoxemia = PaO2 <8.0 kPa, Hypercapnemia = PaCO2 >6.7 kPa, Hypocapnemia = PaCO2 <4.0 kPa. PaO2 no-exposure = 8.0-40 kPa, PaCO2 no-exposure = 4.0-6.7 kPa. Double exposure = hyperoxemia and hypoxemia or hypercapnemia and hypocapnemia.

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| **Supplementary Table 4. Association of exposure to extreme PaO2 and PaCO2 values with poor neurological long term outcome. n = 1850** | | | |
| **Analysis** | **OR** | **95% CI** | **P-Value** |
| Hyperoxemia versus PaO2 no-exposure | 1.29 | 0.85 – 1.95 | 0.23 |
| Hyperoxemia versus no-hyperoxemia | 1.25 | 0.84 – 1.87 | 0.28 |
| Hypoxemia versus PaO2 no-exposure | 1.21 | 0.79 – 1.84 | 0.38 |
| Hypoxemia versus no-hypoxemia | 1.15 | 0.77 – 1.73 | 0.49 |
| Hypercapnemia versus PaCO2 no-exposure | 0.97 | 0.67 – 1.42 | 0.89 |
| Hypercapnemia versus no-hypercapnemia | 0.89 | 0.64 – 1.24 | 0.49 |
| Hypocapnemia versus PaCO2 no-exposure | 1.35 | 0.90 – 2.01 | 0.14 |
| Hypocapnemia versus no-hypocapnemia | 1.29 | 0.92 – 1.82 | 0.14 |

OR = odds ratio, 95% CI = 95% confidence interval, PaO2= arterial partial pressure of oxygen, PaCO2= arterial partial pressure of carbon dioxide. Hyperoxemia = PaO2 >40 kPa, Hypoxemia = PaO2 <8.0 kPa, Hypercapnemia = PaCO2 >6.7 kPa, Hypocapnemia = PaCO2 <4.0 kPa. PaO2 no-exposure = 8.0-40 kPa, PaCO2 no-exposure = 4.0-6.7 kPa.

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| **Supplementary Table 5. Association of exposure to extreme PaO2 and PaCO2 values with poor neurological long term outcome. Imputed values. (n = 2135)** | | | |
| **Analysis** | **OR** | **95% CI** | **P-Value** |
| Hyperoxemia versus PaO2 no-exposure | 1.28 | 0.89 – 1.85 | 0.18 |
| Hyperoxemia versus no-hyperoxemia | 1.18 | 0.83 – 1.68 | 0.35 |
| Hypoxemia versus PaO2 no-exposure | 1.23 | 0.85 – 1.78 | 0.28 |
| Hypoxemia versus no-hypoxemia | 1.15 | 0.81 – 1.65 | 0.43 |
| Hypercapnemia versus PaCO2 no-exposure | 0.91 | 0.65 – 1.28 | 0.59 |
| Hypercapnemia versus no-hypercapnemia | 0.87 | 0.64 – 1.16 | 0.34 |
| Hypocapnemia versus PaCO2 no-exposure | 1.32 | 0.92 – 1.89 | 0.13 |
| Hypocapnemia versus no-hypocapnemia | 1.25 | 0.92 – 1.69 | 0.15 |

OR = odds ratio, 95% CI = 95% confidence interval, PaO2= arterial partial pressure of oxygen, PaCO2= arterial partial pressure of carbon dioxide. Hyperoxemia = PaO2 >40 kPa, Hypoxemia = PaO2 <8.0 kPa, Hypercapnemia = PaCO2 >6.7 kPa, Hypocapnemia = PaCO2 <4.0 kPa, PaO2 no-exposure = 8.0-40 kPa, PaCO2 no-exposure = 4.0-6.7 kPa.

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| **Supplementary Table 6. Baseline characteristics of patients with complete PaO2 and PaCO2 values and patients with PaO2 or PaCO2 missing.** | | |
| **Demographic characteristic** | **PaO2 and PaCO2 complete (n=1891)** | **PaO2 or PaCO2 missing (n=244)** |
|  | **Value** | **Value** |
| Age in years, mean (SD) | 61.01 (15.8) | 61.7 (16.5) |
| Male sex, n (%) | 1270 (67.2) | 162 (66.4) |
| **Medical history** |  |  |
| Previous myocardial infarction n (%) | 342 (18.1) | 28 (11.5) |
| Chronic heart failure n (%) | 321 (17.0) | 46 (18.9) |
| COPD n (%) | 306 (16.2) | 38 (15.6) |
| Cerebro vascular disease n (%) | 171 (9.0) | 25 (10.2) |
| Diabetes mellitus n (%) | 459 (24.3) | 62 (25.4) |
| Obesity n (%) | 241 (15.4) | 27 (14.5) |
| **Cardiac arrest characteristic** |  |  |
| Witnessed cardiac arrest n (%) | 1419 (75.9) | 172 (72.9) |
| Bystander CPR n (%) | 1240 (66.2) | 145 (60.7) |
| Bystander defibrillation n (%) | 113 (6.0) | 10 (4.1) |
| Initial rhythm shockable n (%) | 926 (50.9) | 96 (42.7) |
| Time to ROSC (min), median (IQR) | 29 (21 – 48) | 32 (19 – 53) |
| **Characteristic on arrival** |  |  |
| Sedated on arrival, n (%) | 388 (21.6) | 49 (22.9) |
| GCS Motor 1, n (%) | 1371 (78.9) | 173 (83.2) |
| Circulatory shock on admission, n (%) | 805 (44.0) | 97 (46) |
| Admission pH, median (IQR) | 7.2 (7.1 – 7.3) | 7.2 (7.0 – 7.3) |
| Admission lactate, mmol/l median (IQR) | 6.2 (3.1 – 10.0) | 8.0 (4.1 – 11.3) |
| Bicarbonate on admission, mmol/l, median (IQR) | 18 (14.5 – 21.0) | 18 (15.0 – 22.0) |

n = number, SD = standard deviation, IQR = interquartile range, % = percent, mmol/l = millimole per liter, CPR = cardio pulmonary resuscitation, ROSC = return of spontaneous circulation, COPD = chronic obstructive pulmonary disease, GCS = Glasgow coma scale, PaO2= arterial partial pressure of oxygen, PaCO2= arterial partial pressure of carbon dioxide, all % are presented as valid percent.