# Supplementary material

## Appendix 1. Measurements at 6 hours.

| **Variable** | **Infection (n = 880)** | | **Polytrauma (n = 251)** | | **Other causes (n = 189)** | | **Total (n = 1320)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Living  792 (90.0%) | Deceased  88 (10.0%) | Living  212 (84.5%) | Deceased  39 (15.5%) | Living  163 (86.2%) | Deceased  26 (13.8%) | Living  1167 (88.4%) | Deceased  153 (11.6%) |
| **SBP** | 115 (104-129) | 114 (99-127) | 120 (108-130) | 117 (101-130) | 100 (92-115) | 107 (92-124) | 115 (101-128) | 114 (100-129) |
| **DBP** | 71 (66-80) | 70 (60-79) | 73 (65-80) | 70 (60-81) | 63 (55-72) | 69 (53-72) | 70 (63-80) | 70 (57-78) |
| **MBP** | 87 (80-96) | 84 (72-97) | 89 (81-95) | 85 (75-93) | 76 (68-83) | 80 (66-89) | 87 (78-95) | 85 (71-95) |
| **Pulse pressure** | 43 (34-53) | 40 (33-51) | 45 (38-55) | 43 (36-57) | 38 (30-47) | 40 (32-48) | 43 (34-53) | 40 (34-51) |
| **HR** | 94 (83-104) | 99 (91-105) | 90 (80-100) | 94 (80-107) | 91 (77-100) | 95 (81-110) | 93 (82-103) | 98 (82-105) |
| **RR** | 18 (17-20) | 20 (17-23) | 18 (16-20) | 17 (16-19) | 18 (17-20) | 19 (16-21) | 18 (17-20) | 19 (16-22) |
| **Shock index** | 0.8 (0.7-0.9) | 0.9 (0.7-1.2) | 0.8 (0.6-0.9) | 0.8 (0.6-1) | 0.9 (0.7-1) | 0.9 (0.7-1.1) | 0.8 (0.7-0.9) | 0.9 (0.7-1) |
| **Capillary refill** | 1.8 (1.5-2.1) | 2 (1.7-2.8) | 2 (1.7-2.5) | 2.6 (2-3) | 2 (1.7-2.6) | 2.3 (1.9-2.9) | 1.9 (1.5-2.2) | 2.2 (1.8-2.9) |
| **Temperature °C** | 37 (36.6-37.5) | 36.9 (36.2-37.4) | 36.6 (36-37) | 36.4 (36-36.8) | 36.6 (36.1-37) | 36.6 (36.1-37) | 37 (36.5-37.5) | 36.6 (36-37) |
| **Glasgow** | 15 (15-15) | 15 (14-15) | 15 (13-15) | 6 (3-12) | 15 (15-15) | 15 (12-15) | 15 (15-15) | 15 (13-15) |
| **Lactate Mm/L** | 1.8 (1.3 – 2.4) | 2.3 (1.5 – 3.5) | 2.3 (1.6 – 4) | 5.3 (3.2 – 8.2) | 2 (1.4 – 2.7) | 1.8 (1.6 – 3.8) | 1.8 (1.3 – 2.7) | 2.6 (1.6 – 4.9) |

**HR:** heart rate. **RR:** respiratory rate. **L:** liter. **Mm:** Milimol. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP: systolic blood** pressure.

## Appendix 2. Measurements at 24 hours.

| **Variable** | **Infection (n = 880)** | | **Polytrauma (n = 251)** | | **Other causes (n = 189)** | | **Total (n = 1320)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Living  792 (90.0%) | Deceased  88 (10.0%) | Living  212 (84.5%) | Deceased  39 (15.5%) | Living  792 (90.0%) | Deceased  88 (10.0%) | Living  212 (84.5%) | Deceased  39 (15.5%) |
| **SBP** | 113 (103-125) | 110 (100-124) | 120 (110-131) | 115 (100-128) | 107 (100-119) | 102 (90-112) | 114 (103-126) | 109 (99-123) |
| **DBP** | 70 (63-80) | 67 (56-75) | 72 (67-82) | 67 (60-76) | 67 (60-75) | 62 (53-70) | 70 (63-80) | 66 (56-75) |
| **MBP** | 86 (78-94) | 82 (73-92) | 89 (82-97) | 83 (71-94) | 81 (73-89) | 75 (69-84) | 86 (78-94) | 80 (71-92) |
| **Pulse pressure** | 42 (35-51) | 42 (35-53) | 46 (39-55) | 50 (34-57) | 41 (33-50) | 41 (26-47) | 43 (35-52) | 42 (34-53) |
| **HR** | 90 (79-100) | 97 (84-107) | 89 (78-98) | 95 (82-114) | 88 (75-97) | 92 (77-102) | 90 (78-100) | 95 (83-106) |
| **RR** | 18 (16-20) | 18 (16-22) | 17 (16-20) | 18 (15-20) | 18 (16-20) | 18 (14-22) | 18 (16-20) | 18 (16-21) |
| **Shock index** | 0.8 (0.7-0.9) | 0.9 (0.7-1) | 0.7 (0.6-0.8) | 0.8 (0.7-1) | 0.8 (0.7-0.9) | 0.8 (0.7-1) | 0.8 (0.7-0.9) | 0.8 (0.7-1) |
| **Capillary refill** | 1.6 (1.3-1.9) | 1.9 (1.5-2.3) | 1.8 (1.4-2.1) | 2.5 (2-2.7) | 1.8 (1.5-2.1) | 2 (1.7-3) | 1.6 (1.3-2) | 2 (1.5-2.6) |
| **Temperature °C** | 36.9 (36.5-37.2) | 36.7 (36.7-37.4) | 36.9 (36.4-37.1) | 36.6 (36-37) | 36.5 (36.1-37) | 36.5 (36-36.6) | 36.9 (36.4-37.1) | 36.6 (36.1-37.2) |
| **Glasgow** | 15 (15-15) | 15 (14-15) | 15 (14-15) | 7 (5-12) | 15 (15-15) | 15 (14-15) | 15 (15-15) | 15 (14-15) |
| **Lactate Mm/L** | 1.7 (1.3 – 2.3) | 2.1 (1.6 – 3.5) | 1.7 (1.3 – 2.3) | 2.3 (1.7 – 5.3) | 1.7 (1.3 – 2.3) | 2.2 (1.3 – 3.4) | 1.7 (1.3 – 2.3) | 2.2 (1.6 – 4) |

**HR:** heart rate. **RR:** respiratory rate. **L:** liter. **Mm:** Milimol. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure.

## Appendix 3. Correlation of clinical variables and serum lactate levels.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **First measurement (rho)** | | | | **Delta first and second measurement (rho)** | | | | **Delta first and third measurement (rho)** | | | |
| Infection | Trauma | Others | Total | Infection | Trauma | Others | Total | Infection | Trauma | Others | Total |
| **SBP** | -0.2382 | -0.0426 | -0.0175 | -0.1871 | 0.0202 | 0.1470 | 0.1562 | 0.0774 | 0.0844 | 0.0594 | 0.0359 | 0.1148 |
| **DBP** | -0.1912 | -0.0616 | -0.0787 | -0.1703 | 0.0078 | 0.1693 | 0.1684 | 0.0713 | 0.0388 | 0.0537 | 0.0051 | 0.0686 |
| **MBP** | -0.2264 | -0.0600 | -0.0725 | -0.1899 | 0.0090 | 0.1880 | 0.1874 | 0.0788 | 0.0720 | 0.0718 | 0.0242 | 0.1028 |
| **PP** | -0.1448 | 0.0025 | 0.0828 | -0.1023 | 0.0013 | 0.0194 | 0.0513 | 0.0208 | 0.0733 | 0.0423 | 0.0234 | 0.0859 |
| **HR** | 0.1038 | 0.2028 | 0.0759 | 0.0665 | 0.0720 | - 0.0375 | 0.0475 | 0.0393 | 0.0797 | 0.1026 | 0.1795 | 0.0711 |
| **RR** | 0.1708 | 0.1060 | 0.0965 | 0.1206 | 0.0539 | 0.0990 | 0.1011 | 0.0632 | 0.0267 | 0.0854 | 0.1138 | 0.0337 |
| **Shock index** | 0.2355 | 0.1545 | 0.0414 | 0.1730 | 0.0423 | 0.0947 | 0.1093 | 0.0702 | 0.1205 | 0.1489 | 0.1392 | 0.1385 |
| **Capillary refill time** | 0.2302 | 0.2558 | 0.1959 | 0.2771 | 0.0163 | 0.0863 | 0.0873 | 0.0479 | 0.0618 | 0.1366 | 0.1159 | 0.1069 |
| **Temperature °C** | -0.0442 | -0.0260 | -0.1237 | -0.1705 | -0.0325 | -0.0001 | 0.0188 | 0.0130 | -0.0319 | -0.0333 | 0.0300 | 0.0572 |
| **Glasgow** | -0.1242 | -0.2532 | -0.2656 | -0.2444 | -0.0262 | 0.0682 | 0.1548 | 0.0377 | 0.0163 | 0.0396 | 0.1884 | 0.0867 |

**HR:** heart rate. **RR:** respiratory rate. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure. **PP:** Pulse pressure. **T:** Temperature.

## Appendix 4. Area under the Receiver Operating Characteristic Curve (AUC-ROC) of the first measurements of clinical variables to predict > 2 mmol/L Lactate

| **Variable** | **Infection** | | **Polytrauma** | | **Other causes** | | **Total** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** |
| **SBP** | 0.6116 | 0.57 – 0.65 | 0.4742 | 0.37 – 0.58 | 0.4337 | 0.34 – 0.53 | 0.5876 | 0.55 – 0.62 |
| **DBP** | 0.5827 | 0.54 – 0.62 | 0.5205 | 0.41 – 0.62 | 0.4722 | 0.38 – 0.57 | 0.5767 | 0.54 – 0.61 |
| **MBP** | 0.6053 | 0.57 – 0.64 | 0.4997 | 0.40 – 0.60 | 0.4610 | 0.37 – 0.55 | 0.5898 | 0.55 – 0.62 |
| **Pulse pressure** | 0.5685 | 0.53 – 0.61 | 0.4481 | 0.34 – 0.56 | 0.4216 | 0.33 – 0.51 | 0.5457 | 0.51 – 0.58 |
| **HR** | 0.5411 | 0.50 – 0.58 | 0.5914 | 0.49 – 0.69 | 0.5056 | 0.41 – 0.60 | 0.5235 | 0.49 – 0.56 |
| **RR** | 0.5691 | 0.53 – 0.61 | 0.5017 | 0.39 – 0.61 | 0.5361 | 0.44 – 0.63 | 0.5506 | 0.52 – 0.58 |
| **Shock index** | 0.6034 | 0.57 – 0.64 | 0.5321 | 0.43 – 0.64 | 0.4679 | 0.37 – 0.56 | 0.5763 | 0.54 – 0.61 |
| **Capillary refill** | 0.6095 | 0.57 – 0.65 | 0.5793 | 0.47 – 0.68 | 0.5744 | 0.47 – 0.68 | 0.6229 | 0.59 – 0.66 |
| **Temperature °C** | 0.5259 | 0.49 – 0.56 | 0.4792 | 0.37 – 0.59 | 0.5217 | 0.42 – 0.62 | 0.5712 | 0.54 – 0.60 |
| **Glasgow** | 0.5366 | 0.51 – 0.56 | 0.6180 | 0.52 – 0.71 | 0.5635 | 0.49 – 0.63 | 0.5692 | 0.55 – 0.59 |

**HR:** heart rate. **RR:** respiratory rate. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure.

## Appendix 5. AUC-ROC of changes between the first and second measurements of clinical variables to predict any lactate clearance.

| **Variable** | **Infection** | | **Polytrauma** | | **Other causes** | | **Total** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** |
| **Delta of SBP 6-0 hours** | 0.5036 | 0.46– 0.55 | 0.5790 | 0.49 – 0.67 | 0.5967 | 0.50 – 0.69 | 0.5290 | 0.49 – 0.67 |
| **Delta of DBP 6-0 hours** | 0.4927 | 0.45 – 0.54 | 0.5668 | 0.48 – 0.66 | 0.6182 | 0.52 – 0.71 | 0.5248 | 0.49 – 0.56 |
| **Delta of MBP 6-0 hours** | 0.4906 | 0.45 – 0.53 | 0.5865 | 0.50 – 0.67 | 0.6223 | 0.53 – 0.71 | 0.5262 | 0.49 – 0.56 |
| **Delta of Pulse pressure 6-0 hours** | 0.5098 | 0.47 – 0.55 | 0.5223 | 0.43 – 0.62 | 0.5283 | 0.43 – 0.62 | 0.5151 | 0.49 – 0.55 |
| **Delta of HR 0-6 horas** | 0.4545 | 0.41 – 0.50 | 0.5290 | 0.44 – 0.61 | 0.4958 | 0.39 – 0.60 | 0.4726 | 0.44 – 0.51 |
| **Delta of RR 0-6 horas** | 0.4779 | 0.43 – 0.52 | 0.4449 | 0.35 – 0.54 | 0.4270 | 0.32 – 0.54 | 0.4671 | 0.43 – 0.50 |
| **Delta of Shock index 0-6 horas** | 0.4778 | 0.44 – 0.52 | 0.4625 | 0.37 – 0.55 | 0.4577 | 0.36 – 0.56 | 0.4699 | 0.43 – 0.51 |
| **Delta of Capillary refill 0-6 horas** | 0.4758 | 0.43 – 0.52 | 0.4419 | 0.35 – 0.53 | 0.4595 | 0.35 – 0.57 | 0.4625 | 0.43 – 0.50 |
| **Delta of Temperature 6-0 hours** | 0.4899 | 0.45 – 0.53 | 0.4964 | 0.41 – 0.59 | 0.5913 | 0.49 – 0.69 | 0.4992 | 0.46 – 0.54 |
| **Delta of Glasgow 6-0 hours** | 0.4990 | 0.48 – 0.52 | 0.5351 | 0.46 – 0.61 | 0.5559 | 0.50 – 0.61 | 0.4875 | 0.47 – 0.51 |

**HR:** heart rate. **RR:** respiratory rate. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure.

## Appendix 6. AUC-ROC of changes between the first and second measurements of clinical variables to predict a 10% lactate clearance.

| **Variable** | **Infection** | | **Polytrauma** | | **Other causes** | | **Total** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** |
| **Delta of SBP 6-0 hours** | 0.5050 | 0.46 – 0.55 | 0.6020 | 0.52 – 0.69 | 0.5546 | 0.46 – 0.65 | 0.5300 | 0.50 – 0.56 |
| **Delta of DBP 6-0 hours** | 0.4932 | 0.45 – 0.53 | 0.5824 | 0.50 – 0.69 | 0.6244 | 0.53 – 0.72 | 0.5296 | 0.50 – 0.56 |
| **Delta of MBP 6-0 hours** | 0.4928 | 0.45 – 0.53 | 0.6044 | 0.52 – 0.69 | 0.6169 | 0.53 – 0.71 | 0.5311 | 0.50 – 0.57 |
| **Delta of Pulse pressure 6-0 hours** | 0.5037 | 0.46 – 0.54 | 0.5481 | 0.46 – 0.64 | 0.4756 | 0.38 – 0.57 | 0.5081 | 0.47 – 0.54 |
| **Delta of HR 0-6 horas** | 0.4575 | 0.42 – 0.50 | 0.5349 | 0.45 – 0.62 | 0.4626 | 0.37 – 0.56 | 0.4709 | 0.44 – 0.51 |
| **Delta of RR 0-6 horas** | 0.4722 | 0.43 – 0.51 | 0.4250 | 0.33 – 0.51 | 0.4306 | 0.33 – 0.53 | 0.4600 | 0.43 – 0.49 |
| **Delta of Shock index 0-6 horas** | 0.4815 | 0.44 – 0.52 | 0.4524 | 0.36 – 0.54 | 0.4999 | 0.36 – 0.54 | 0.4693 | 0.44 – 0.50 |
| **Delta of Capillary refill 0-6 horas** | 0.4863 | 0.44 – 0.53 | 0.4828 | 0.39 – 0.57 | 0.4305 | 0.33 – 0.53 | 0.4746 | 0.44 – 0.51 |
| **Delta of Temperature 6-0 hours** | 0.4938 | 0.45 – 0.53 | 0.4789 | 0.39 – 0.57 | 0.6121 | 0.52 – 0.70 | 0.5058 | 0.47 – 0.54 |
| **Delta of Glasgow 6-0 hours** | 0.4990 | 0.48 – 0.51 | 0.4984 | 0.42 – 0.57 | 0.5592 | 0.51 – 0.61 | 0.5082 | 0.49 – 0.52 |

**HR:** heart rate. **RR:** respiratory rate. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure.

## Appendix 7. AUC-ROC of changes between the first and second measurements of clinical variables to predict a 50% lactate clearance.

| **Variable** | **Infection** | | **Polytrauma** | | **Other causes** | | **Total** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** | **Area** | **95% CI** |
| **Delta of SBP 6-0 hours** | 0.5200 | 0.47 – 0.57 | 0.6397 | 0.55 – 0.73 | 0.5464 | 0.44 – 0.65 | 0.5517 | 0.51 – 0.59 |
| **Delta of DBP 6-0 hours** | 0.5050 | 0.46 – 0.56 | 0.6479 | 0.55 – 0.74 | 0.5016 | 0.40 – 0.60 | 0.5350 | 0.49 – 0.58 |
| **Delta of MBP 6-0 hours** | 0.5112 | 0.46 – 0.56 | 0.6606 | 0.57 – 0.75 | 0.5316 | 0.42 – 0.64 | 0.5465 | 0.51 – 0.59 |
| **Delta of Pulse pressure 6-0 hours** | 0.5095 | 0.46 – 0.56 | 0.5348 | 0.44 – 0.63 | 0.5479 | 0.44 – 0.66 | 0.5247 | 0.48 – 0.57 |
| **Delta of HR 0-6 horas** | 0.4303 | 0.38 – 0.48 | 0.4489 | 0.35 – 0.55 | 0.4612 | 0.36 – 0.57 | 0.4421 | 0.40 – 0.48 |
| **Delta of RR 0-6 horas** | 0.4859 | 0.44 – 0.54 | 0.4264 | 0.32 – 0.53 | 0.4698 | 0.37 – 0.57 | 0.4750 | 0.43 – 0.52 |
| **Delta of Shock index 0-6 horas** | 0.4596 | 0.41 – 0.51 | 0.3637 | 0.27 – 0.46 | 0.4747 | 0.37 – 0.58 | 0.4419 | 0.40 – 0.48 |
| **Delta of Capillary refill 0-6 horas** | 0.5105 | 0.46 – 0.56 | 0.4361 | 0.33 – 0.54 | 0.5135 | 0.41 – 0.62 | 0.4958 | 0.45 – 0.54 |
| **Delta of Temperature 6-0 hours** | 0.4568 | 0.41 – 0.51 | 0.4443 | 0.33 – 0.56 | 0.5819 | 0.48 – 0.68 | 0.4829 | 0.44 – 0.53 |
| **Delta of Glasgow 6-0 hours** | 0.4869 | 0.47 – 0.51 | 0.5337 | 0.45 – 0.62 | 0.5380 | 0.47 – 0.60 | 0.5044 | 0.48 – 0.53 |

**HR:** heart rate. **RR:** respiratory rate. **DBP:** diastolic blood pressure. **MBP:** mean blood pressure. **SBP:** systolic blood pressure.