**S-table 1**: Additional demographics and clinical parameters in cardiovascular subphenotypes.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Parameter | All  n = 801 | Class 1  n = 347 | Class 2  n = 188 | Class 3  n = 102 | Class 4  n = 164 | P value |
| **Demographics** |  |  |  |  |  |  |
| Performance status | 1 (1 – 2) | 1 (1 – 2) | 1 (1 – 2) | 1 (1 – 2) | 1 (1 – 2) | 0.066 |
| Comorbidities |  |  |  |  |  | 0.209 |
| Diabetes mellitus | 118 (14.7) | 58 (16.7) | 25 (13.3) | 15 (14.7) | 20 (12.2) |  |
| Obesity | 178 (22.2) | 84 **(**24.2) | 37 (19.7) | 29 (28.4) | 28 (17.1) |  |
| Cancer | 144 (18.0) | 60 (17.3) | 34 (18.1) | 19 (18.6) | 31 (18.9) |  |
| Hypertension | 191 (23.9) | 96 (27.7) | 23 (12.2) | 36 (35.3) | 36 (22.0) |  |
| Ischaemic heart disease | 115 (14.4) | 63 (18.2) | 19 (10.1) | 16 (15.7) | 17 (10.4) |  |
| Chronic obstructive pulmonary disease / Asthma | 134 (16.7) | 65 (18.7) | 28 (14.9) | 20 (19.6) | 21 (12.8) |  |
| Chronic kidney disease | 95 (11.9) | 43 (12.4) | 16 (8.5) | 12 (11.8) | 24 (14.6) |  |
| Liver disease | 120 (15.0) | **32** (9.2) | 36 (19.1) | 11 (10.8) | 41 (25.0) |  |
| TIA / Stroke | 72 (9.0) | 43 (12.4) | 8 (4.3) | 6 (5.9) | 15 (9.2) |  |
| None | 181 (22.6) | **70** (20.2) | 59 (31.4) | 20 (19.6) | 32 (19.5) |  |
| **Clinical variables** |  |  |  |  |  |  |
| Vasopressin n (%) | 117 (14.6) | 36 (10.4) | 19 (10.1) | 25 (24.5) | 37 (22.2) | <0.0001 |
| Inotrope n (%) | 56 (7.0) | 24 (6.9) | 9 (4.8) | 17 (16.7) | 6 (3.6) | 0.0003 |
| 2nd vasoactive agent | 178 (22.2) | 62 (17.9) | 30 (16.0) | 42 (41.8) | 44 (26.8) | <0.0001 |
| Total fluid input on day; mLs | 420 (210 – 810) | 420 (200 – 830) | 460 (280 – 890) | 300 (150 – 560) | 440 (210 – 880) | 0.0053 |
| Cumulative fluid balance; mLs | -730 (-70 – -1540) | -860 (-270 – -1670) | -870 (-120 – -1630) | -470 (+80 – -1140) | -520 (+110 – -1500) | 0.0002 |
| Temperature | 36.7 (36.1 – 37.2) | 36.7 (36.2 – 37.3) | 36.6 (36.2 – 37.1) | 36.3 (35.9 – 36.9) | 36.9 (36.2 – 37.5) | <0.0001 |
| White blood cell count; x 109 L-1 (n=777) | 12.8 (9.2 – 18.0) | 12.8 (9.4 – 17.7) | 11.4 (8.6 – 16.3) | 13.4 (9.4 – 18.3) | 14.6 (9.7 – 20.0) | 0.0047 |
| C-reactive protein; mg mL-1 (n=776) | 105 (48 – 205) | 109 (47 – 205) | 96 (54 – 175) | 98 (46 – 215) | 110 (47 – 237) | 0.627 |
| Ventilation rate; bpm (n=691) | 20 (18 – 22) | 18 (16 – 21) | 19 (17 – 22) | 20 (17 – 22) | 20 (18 – 22) | 0.051 |
| HS Troponin (n=82) | 71 (16 – 630) | 37 (11 – 1083) | 36 (1 – 256) | 57 (23 – 429) | 540 (59 – 6078) | 0.279 |
| Neutrophils x 109 L-1 (n=776) | 10 (7 – 15) | 10 (7 – 15) | 9 (6 – 13) | 11 (7 – 15) | 12 (8 – 16) | 0.0077 |
| Lymphocytes x 109 L-1 (n=776) | 1 (0.6 – 1.5) | 1 (0.6 – 1.6) | 1 (0.6 – 1.4) | 0.9 (0.7 – 1.7) | 1.1 (0.6 – 1.6) | 0.590 |
| Bilirubin mol L-1 (n=776) | 13 (8 – 30) | 11 (7 – 21) | 14 (8 – 33) | 17 (9 – 30) | 16 (10 – 60) | <0.0001 |
| Alanine transaminase; IUL-1 (n=776) | 39 (22 – 88) | 36 (20 – 83) | 39 (24 – 74) | 43 (18 – 116) | 46 (24 – 113) | 0.242 |
| Alkaline phosphatase; IU L-1 (n=776) | 101 (67 – 156) | 98 (66 – 154) | 94 (64 – 138) | 109 (73 – 175) | 115 (73 – 172) | 0.201 |
| Albumin g dL-1 (n=776) | 27 (23 – 31) | 27 (24 – 31) | 28 (24 – 31) | 27 (23 – 31) | 27 (23 – 32) | 0.659 |
| Creatinine mg/dL (n=776) | 86 (58 – 141) | 81 (56–127) | 86 (56–149) | 105 (70–171) | 85 (61–136) | <0.0001 |
| Lactate mmol L-1 | 1.5 (1.1 – 2.3) | 1.4 (1 – 1.9) | 1.3 (1 – 1.9) | 1.9 (1 – 2.9) | 2 (1.2 – 3.3) | <0.0001 |
| Platelets x 109 L-1 (n=776) | 179 (101 – 273) | 201 (124–287) | 168 (85 – 247) | 177 (104–279) | 159 (76 – 257) | 0.0015 |
| INR (n=776) | 1.2 (1.1–1.4) | 1.2 (1.1–1.4) | 1.2 (1.1–1.4) | 1.2 (1.1–1.7) | 1.3 (1.1–1.7) | <0.0001 |
| **Echocardiographic parameters** |  |  |  |  |  |  |
| RVEDAi; cm2.m-2 | 9.7 (8.0 – 12.0) | 9.1 (7.9 – 10.6) | 11.8 (9.5 – 14.5) | 13.6 (10.9 – 15.8) | 7.9 (6.5 – 9.6) | <0.0001 |
| RVESAi*;* cm2.m-2 | 5.6 (4.4 – 7.6) | 5.3 (4.5 – 6.3) | 6.5 (5.3 – 8.8) | 10.0 (8.4 – 12.0) | 4.1 (3.1 – 5.1) | <0.0001 |
| LVEDAi; cm2.m-2 | 16.5 (14.1 – 18.8) | 17.1 (15.0 – 19.7) | 17.1 (14.2 – 19.1) | 14.5 (12.6 – 16.6) | 15.4 (12.5 – 17.7) | <0.0001 |
| LVESAi; cm2.m-2 | 9.6 (7.2 – 11.9) | 10.5 (8.5 – 12.9) | 9.7 (7.3 – 12.3) | 9.2 (6.8 – 11.4) | 7.3 (5.5 – 9.8) | <0.0001 |
| **Diastolic dysfunction (n=608)** |  |  |  |  |  |  |
| Peak mitral inflow E/A velocity by pulse wave Doppler | 1.0 (0.8 – 1.3) | 1.1 (0.9 – 1.3) | 1.0 (0.9 – 1.3) | 0.9 (0.8 – 1.2) | 1.0 (0.8 – 1.1) | 0.0003 |
| E/E’ | 8.7 (7.0 – 10.0) | 8.9 (7.0 – 10.4) | 8.7 (6.5 – 10.0) | 8.0 (7.0 – 10.0) | 9.0 (7.0 – 10.0) | 0.656 |
| Diastolic peak velocity of lateral mitral valve by tissue Doppler imaging | 10.0 (9.0 – 12.1) | 10.2 (9.0 – 12.1) | 10.7 (9.2 – 12.9) | 9.3 (8.0 – 11.4) | 10.0 (9.0 – 12.0) | 0.0122 |
| Right ventricular systolic impairment severity |  |  |  |  |  | <0.0001 |
| Mild (25 – 35) | 170 (21.2) | 65 (18.7) | 48 (25.5) | 32 (31.4) | 25 (15.2) |  |
| Moderate (18 – 24.9) | 43 (5.4) | 10 (2.9) | 4 (2.1) | 29 (28.4) | 0 |  |
| Severe (<18) | 34 (4.3) | 0 | 0 | 34 (33.3) | 0 |  |
| Impaired Tricuspid annular plane systolic excursion | 139 (17.4) | 37 (10.7) | 23 (12.2) | 63 (61.8) | 16 (9.8) |  |
| Right ventricular dilation severity |  |  |  |  |  | <0.0001 |
| Mild (0.6 – 0.8) | 211 (26.3) | 33 (9.5) | 115 (61.2) | 32 (31.4) | 31 (18.9) |  |
| Moderate (0.8 – 1.0) | 80 (10.0) | 0 | 48 (25.5) | 32 (31.4) | 0 |  |
| Severe (≥1.0) | 44 (5.5) | 0 | 8 (4.3) | 36 (35.3) | 0 |  |
| Left ventricular systolic impairment grade |  |  |  |  |  | 0.215 |
| Mild (45-54%) | 42 (5.2) | 22 (6.3) | 8 (4.3) | 11 (10.8) | 1 (0.6) |  |
| Moderate (36 – 44%) | 36 (4.5) | 26 (7.5) | 5 (2.7) | 4 (3.9) | 1 (0.6) |  |
| Severe (≤35%) | 44 (5.5) | 25 (7.2) | 3 (1.6) | 13 (12.8) | 3 (1.8) |  |
| LVOT VTI (n=792) | 24.0 (19.6 – 29.1) | 22.8 (19.0 – 25.8) | 25.5 (20.8 – 30.1) | 17.0 (13.0 – 23.0) | 30.0 (25.0 – 35.3) | <0.0001 |

s-table 1 legend: Values are number (proportion) or median (IQR). INR = international normalised TIA = transient ischaemic attack. PBW = predicted body weight. HS = high sensitiity

**s-Table 2** Comparison of demographics and clinical variables in survivors and non-survivors

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Survived  (n=482) | Died  (n=319) | P value |
| Age; years | 60 (47 – 70) | 66 (53 – 77) | <0.0001 |
| Sex; % male | 306 (63.4) | 202 (63.3) | 0.963 |
| Day of transthoracic echocardiogram | 3 (2 – 6) | 4 (2 – 7) | 0.336 |
| ARDS severity |  |  | 0.00012 |
| Mild | 270 (56.0) | 131 (41.1) |  |
| Moderate | 202 (41.9) | 175 (54.9) |  |
| Severe | 10 (2.1) | 13 (4.1) |  |
| SOFA score | 6 (3 – 8) | 10 (7 – 13) | <0.0001 |
| Tracheal intubation | 406 (84.2) | 285 (89.3) | 0.0397 |
| Initial risk factor for ARDS |  |  | 0.241 |
| Pneumonia | 249 (51.7) | 171 (53.6) |  |
| Non-respiratory Sepsis | 117 (24.3) | 91 (28.5) |  |
| Chest trauma | 70 (14.5) | 31 (9.7) |  |
| Aspiration | 34 (7.1) | 20 (6.6) |  |
| Other | 12 (2.5) | 6 (1.9) |  |
| **Clinical** |  |  |  |
| PaO2:FiO2 ratio | 29 (22 – 34) | 25 (20 – 31) | <0.0001 |
| PaCO2; kpa | 5.9 (5.1 – 6.9) | 6.1 (5.2 – 7.1) | 0.080 |
| pH | 7.38 (7.33 – 7.44) | 7.36 (7.31 – 7.42) | 0.056 |
| White blood cell count; x 109 L-1 | 13 (9 – 17) | 13 (9 – 19) | 0.376 |
| C-reactive protein; mg mL-1 | 105 (48 – 203) | 105 (49 – 213) | 0.382 |
| Chest radiograph opacification score (0-16) | 6 (4 – 8) | 6 (4 – 8) | 0.095 |
| Deadspace fraction | 0.62 (0.55 – 0.69) | 0.64 (0.55 – 0.72) | 0.171 |
| Dynamic compliance; mLs cm H2O-1 | 30 (26 – 37) | 29 (25 – 34) | 0.107 |
| Peak airway pressure; cm H2O | 23 (20 – 27) | 23 (20 – 27) | 0.810 |
| Positive end expiratory pressure; cm H2O | 7 (5 – 8) | 7 (5 – 8) | 0.436 |
| Urine output; mLs kg-1 hour-1 | 0.8 (0.4 – 1.2) | 0.4 (0.1 – 0.9) | <0.0001 |
| Renal replacement therapy | 86 (17.8) | 124 (38.8) | <0.0001 |

|  |  |  |  |
| --- | --- | --- | --- |
| Performance status | 1 (0 – 1) | 1 (1 – 2) | 0.0003 |
| Charlson Comorbidity index | 4 (2 – 5) | 4 (3 – 5) | 0.0168 |
| Comorbidities |  |  | 0.0057 |
| Diabetes mellitus | 74 (9.5) | 44 (13.8) |  |
| Obesity | 43 (5.5) | 46 (14.4) |  |
| Cancer | 66 (8.4) | 76 (23.8) |  |
| Hypertension | 119 (24.7) | 72 (22.6) |  |
| Ischaemic heart disease | 68 (14.1) | 47 (14.7) |  |
| Chronic obstructive pulmonary disease / Asthma | 86 (17.8) | 48 (15.1) |  |
| Chronic kidney disease | 53 (11.0) | 42 (13.2) |  |
| Liver disease | 61 (12.7) | 59 (18.5) |  |
| TIA / Stroke | 55 (11.4) | 17 (5.3) |  |
| None | 124 (25.7) | 57 (17.9) |  |
| BMI kg m-2 | 28 (24 – 32) | 27 (23 – 31) | 0.125 |
| **Clinical variables** |  |  |  |
| Mean tidal volume; mls/kg/PBW | 5.9 (5.1 – 6.9) | 5.8 (5.0 – 6.7) | 0.248 |
| Total fluid input; mLs | 420 (210 – 850) | 420 (210 – 760) | 0.457 |
| Cumulative fluid balance; mLs | -970 (-370 – -1740) | -330 (-130 – -1180) | <0.0001 |
| Temperature | 36.8 (36.3 – 37.2) | 36.5 (35.9 – 37.1) | <0.0001 |
| Ventilation rate; bpm | 20 (18 – 22) | 20 (18 – 22) | 0.449 |
| HS Troponin (n=82) | 95 (23 – 571) | 251 (34 – 2402) | 0.335 |
| D-dimer (n=26) | 2070 (380 – 4200) | 1970 (380 – 7100) | 0.873 |
| Neutrophils x 109 L-1 | 10 (7 – 14) | 11 (7 – 16) | 0.408 |
| Lymphocytes x 109 L-1 | 1 (0.7 – 1.6) | 0.9 (0.5 – 1.4) | 0.015 |
| Bilirubin mol L-1 | 11 (6 – 17) | 22 (11 – 61) | <0.0001 |
| Alanine transaminase; IUL-1 | 38 (21 – 82) | 41 (22 – 93) | 0.568 |
| Alkaline phosphatase; IU L-1 | 94 (66 – 140) | 116 (72 – 177) | 0.0036 |
| Albumin g dL-1 | 28 (23 – 31) | 27 (23 – 31) | 0.213 |
| Creatinine mg/dL | 78 (55 – 120) | 104 (69 – 160) | <0.0001 |
| Lactate mmol L-1 | 1.3 (1 – 1.9) | 1.7 (1.2 – 2.8) | <0.0001 |
| Platelets x 109 L-1 | 201 (130 – 295) | 143 (69 – 248) | <0.0001 |
| INR | 1.2 (1.1 – 1.3) | 1.3 (1.1 – 1.6) | <0.0001 |

**s-Table 3** Association between cardiovascular subphenotype and mortality following multivariate logistic regression analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **CV phenotype** | Prevalence | 90-day mortality rate | OR (95% CI) | P value |
| **LCA derived** |  |  |  |  |
| Class 1 | 43.3% | 19.4% (67/347) | 0.20 (0.14 – 0.29) | <0.001 |
| Class 2 | 23.5% | 39.7% (75/188) | 1.05 (0.72 – 1.54) | 0.794 |
| Class 3 | 12.7% | 78.4% (80/102) | 6.86 (3.97 – 11.83) | <0.001 |
| Class 4 | 20.5% | 59.1% (97/164) | 2.47 (1.64 – 3.72) | <0.001 |
| **RV TTE derived** |  |  |  |  |
| RV dilation & impairment | 19.7% | 70.3% (111/158) | 6.00 (3.87 – 9.31) | <0.001 |
| RV dilation w normal function | 21.7% | 36.8% (64/174) | 0.72 (0.48 – 1.07) | 0.103 |
| RVSD w normal size | 11.2% | 30.0% (27/90) | 0.68 (0.40 – 1.17) | 0.162 |
| Normal RV size and function | 47.3% | 30.9% (117/379) | 0.47 (0.34 – 0.66) | <0.001 |
| **Other RVD definitions** |  |  |  |  |
| Acute cor pulmonale | 11.6% | 57.0% (53/93) | 2.42 (1.40 – 4.18) | 0.002 |
| RV dilation + CVP>8 | 25.7% | 52.0% (107/206) | 1.69 (1.17 – 2.43) | 0.005 |
| RV dilation | 41.5% | 52.7% (175/332) | 2.49 (1.79 – 3.47) | <0.001 |
| RVSD | 31.0% | 55.7% (138/248) | 3.13 (2.19 – 4.47) | <0.001 |

s-Table 3 Legend = LCA = latent class analysis. RV = right ventricular. TTE = transthoracic echocardiography. RVSD = right ventricular systolic dysfunction. CVP = central venous pressure. RVD = right ventricular dysfunction. OR = odds ratio.