**Blood and urinary cytokine balance and renal outcomes at cardiac surgery**

William T. McBride MD1, Mary Jo Kurth PhD2, Anna Domanska PhD2, Joanne Watt MSc2,Gavin McLean MD1, Jijin Joseph MD1, John V. Lamont MSc2, Peter Fitzgerald PhD2 and Mark W. Ruddock PhD2\*.

Affiliations

1Department of Cardiac Anesthesia, Belfast Health & Social Care Trust, 274 Grosvenor Road, Belfast BT12 6BA, Northern Ireland, UK

2Randox Laboratories Ltd, Clinical Studies Group, 55 Diamond Road, Crumlin, County Antrim BT29 4QY, Northern Ireland, UK

\*Corresponding author

Mark W. Ruddock

Randox Laboratories Ltd, Clinical Studies Group, 55 Diamond Road, Crumlin, County Antrim BT29 4QY, Northern Ireland, UK

Tele: +44 (0)28 9442 2413

Fax: +44 (0)28 9445 2912

Email: [mark.ruddock@randox.com](mailto:mark.ruddock@randox.com)

Supplemental Table 1. Blood pro-inflammatory and anti-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood**  **cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| sIP-10 | pre-op | 289 | 114.27 | 25 | 156.80 | 0.014 |
| sIP-10 | post-op | 284 | 101.27 | 25 | 160.30 | 0.048 |
| sIL-12p40 | post-op | 284 | 286.39 | 25 | 385.52 | 0.039 |
| sMK | post-op | 243 | 1060.00 | 21 | 1905.26 | 0.050 |
| pIL-6 | pre-op | 283 | 2.20 | 25 | 3.54 | 0.003 |
| pMIP-1α | pre-op | 280 | 3.62 | 25 | 4.58 | 0.008 |
| pMIP-1α | post-op | 286 | 4.60 | 25 | 7.31 | 0.006 |
| pMCP-1 | pre-op | 283 | 130.00 | 25 | 142.00 | 0.032 |
| pMCP-1 | post-op | 289 | 203.00 | 25 | 299.00 | 0.009 |
| pNGAL | post op | 290 | 975.05 | 25 | 1303.85 | 0.019 |
| pTNFα | post-op | 289 | 2.36 | 25 | 3.14 | 0.037 |
| **Anti-inflammatory cytokines** | | | | | | |
| sTNFsr1 | pre-op | 289 | 0.35 | 25 | 0.50 | <0.001 |
| sTNFsr1 | post-op | 284 | 0.70 | 25 | 1.08 | <0.001 |
| sTNFsr2 | pre-op | 289 | 0.37 | 25 | 0.57 | 0.015 |
| sTNFsr2 | post-op | 284 | 0.73 | 25 | 1.26 | <0.001 |
| sIL-1RA | pre-op | 289 | 63.46 | 25 | 102.26 | 0.017 |
| sIL-1RA | post-op | 284 | 429.36 | 25 | 650.93 | 0.032 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sIP-10 – serum interferon gamma - induced protein-10, sIL-12p40 – serum interleukin-12 subunit p40, sMK – serum midkine, pIL-6 – plasma interleukin-6, pMIP-1α – plasma macrophage inflammatory protein-1α, pMCP-1 – plasma monocyte chemotactic protein-1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, pTNFα – plasma tumour necrosis factor α, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist

Supplemental Table 2. Urinary pro-inflammatory and anti-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| uIP-10 | post-op | 286 | 13.12 | 25 | 25.99 | 0.001 |
| uNGAL | post-op | 276 | 144.01 | 25 | 227.39 | 0.001 |
| **Anti-inflammatory cytokines** | | | | | | |
| uTNFsr2 | post-op | 285 | 8.18 | 25 | 9.75 | 0.027 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uIP-10 – urinary interferon gamma - induced protein-10, uNGAL – urinary neutrophil gelatinase-associated lipocalin, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2

Supplemental Table 3. Blood pro-inflammatory and anti-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood**  **cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| sIP-10 | pre-op | 275 | 114.50 | 55 | 137.14 | 0.043 |
| sIL-12p40 | pre-op | 275 | 371.19 | 55 | 539.87 | <0.001 |
| sIL-12p40 | post-op | 269 | 273.87 | 56 | 438.05 | <0.001 |
| sMK | post-op | 224 | 990.10 | 50 | 2412.33 | <0.001 |
| pIL-6 | pre-op | 269 | 2.24 | 55 | 2.92 | 0.007 |
| pIL-8 | post-op | 274 | 9.01 | 56 | 11.44 | 0.036 |
| pMIP-1α | pre-op | 266 | 3.61 | 55 | 4.45 | 0.012 |
| pMIP-1α | post-op | 271 | 4.52 | 56 | 6.41 | <0.001 |
| pMCP-1 | pre-op | 269 | 130.00 | 55 | 140.00 | 0.034 |
| pMCP-1 | post-op | 274 | 198.00 | 56 | 234.50 | 0.006 |
| pNGAL | pre-op | 270 | 573.54 | 55 | 672.83 | 0.002 |
| pNGAL | post op | 275 | 964.87 | 56 | 1463.26 | <0.001 |
| pTNFα | pre-op | 269 | 2.06 | 55 | 2.55 | 0.001 |
| pTNFα | post-op | 274 | 2.34 | 56 | 3.04 | 0.001 |
| **Anti-inflammatory cytokines** | | | | | | |
| sTNFsr1 | pre-op | 275 | 0.33 | 55 | 0.54 | <0.001 |
| sTNFsr1 | post-op | 269 | 0.69 | 56 | 1.03 | <0.001 |
| sTNFsr2 | pre-op | 275 | 0.36 | 55 | 0.57 | <0.001 |
| sTNFsr2 | post-op | 269 | 0.73 | 56 | 1.20 | <0.001 |
| sIL-1RA | pre-op | 275 | 62.37 | 55 | 84.29 | 0.015 |
| sIL-1RA | post-op | 269 | 414.26 | 56 | 701.17 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sIP-10 – serum interferon gamma - induced protein-10, sIL-12p40 – serum interleukin-12 subunit p40, sMK – serum midkine, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin-8, pMIP-1α – plasma macrophage inflammatory protein-1α, pMCP-1 – plasma monocyte chemotactic protein-1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, pTNFα – plasma tumour necrosis factor α, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist

Supplemental Table 4. Urinary pro-inflammatory and anti-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| uIP-10 | pre-op | 273 | 5.50 | 56 | 9.42 | 0.031 |
| uIP-10 | post-op | 271 | 13.51 | 56 | 21.08 | 0.012 |
| uIL-12p40 | pre-op | 273 | 1.99 | 56 | 2.66 | 0.028 |
| uIL-12p40 | post-op | 271 | 2.90 | 56 | 4.82 | <0.001 |
| uNGAL | post-op | 262 | 141.19 | 55 | 230.31 | 0.002 |
| **Anti-inflammatory cytokines** | | | | | | |
| uTNFsr1 | pre-op | 272 | 0.52 | 56 | 0.71 | 0.026 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uIP-10 – urinary interferon gamma - induced protein-10, uIL-12p40 – urinary interleukin-12 subunit p40, uNGAL – urinary neutrophil gelatinase-associated lipocalin, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1

Supplemental Table 5. Blood pro-inflammatory and anti-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood**  **cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| sIL-12p40 | pre-op | 298 | 388.51 | 22 | 712.18 | <0.001 |
| sIL-12p40 | post-op | 293 | 293.16 | 22 | 444.80 | 0.003 |
| sMK | post-op | 248 | 1063.82 | 18 | 2651.94 | 0.010 |
| pIL-6 | pre-op | 292 | 2.24 | 22 | 3.05 | 0.030 |
| pIL-8 | post-op | 298 | 8.99 | 22 | 14.57 | 0.010 |
| pMIP-1α | pre-op | 289 | 3.62 | 22 | 4.71 | 0.002 |
| pMIP-1α | post-op | 295 | 4.79 | 22 | 7.30 | 0.003 |
| pMCP-1 | pre-op | 292 | 129.55 | 22 | 154.50 | 0.017 |
| pMCP-1 | post-op | 298 | 202.50 | 22 | 255.57 | 0.026 |
| pNGAL | pre-op | 293 | 580.62 | 22 | 832.09 | 0.004 |
| pNGAL | post op | 299 | 978.72 | 22 | 1509.05 | 0.001 |
| pTNFα | pre-op | 292 | 2.06 | 22 | 2.66 | 0.002 |
| pTNFα | post-op | 298 | 2.37 | 22 | 3.15 | 0.008 |
| **Anti-inflammatory cytokines** | | | | | | |
| sTNFsr1 | pre-op | 298 | 0.35 | 22 | 0.56 | <0.001 |
| sTNFsr1 | post-op | 293 | 0.70 | 22 | 1.10 | <0.001 |
| sTNFsr2 | pre-op | 298 | 0.37 | 22 | 0.55 | <0.001 |
| sTNFsr2 | post-op | 293 | 0.74 | 22 | 1.26 | <0.001 |
| sIL-1RA | post-op | 293 | 430.69 | 22 | 1066.10 | 0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sIL-12p40 – serum interleukin-12 subunit p40, sMK – serum midkine, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, pMIP-1α – plasma macrophage inflammatory protein-1α, pMCP-1 – plasma monocyte chemotactic protein 1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, pTNFα – plasma tumour necrosis factor α, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin -1 receptor antagonist

Supplemental Table 6. Urinary pro-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Pro-inflammatory cytokines** | | | | | | |
| uIP-10 | post-op | 295 | 13.23 | 22 | 26.55 | 0.019 |
| uIL-12p40 | pre-op | 297 | 1.88 | 22 | 3.13 | 0.003 |
| uIL-12p40 | post-op | 295 | 3.07 | 22 | 4.50 | 0.040 |
| uNGAL | post-op | 286 | 145.89 | 21 | 241.82 | 0.010 |

pre-op – preoperative, post-op – postoperative, CS-AKI –cardiac surgery acute kidney injury, n – number of patients, uIP-10 – urinary interferon gamma - induced protein-10, uIL-12p40 – urinary interleukin-12 subunit p40, uNGAL – urinary neutrophil gelatinase-associated lipocalin

Supplemental Table 7. Ratios of blood anti-inflammatory/blood pro-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ pTNFα | pre-op | 237 | 0.158 | 23 | 0.207 | 0.005 |
| sTNFsr1/ pTNFα | post-op | 240 | 0.272 | 23 | 0.326 | 0.038 |
| sTNFsr1/ pIL-6 | post-op | 280 | 0.006 | 25 | 0.011 | 0.014 |
| sTNFsr1/sIL-12p40 | post-op | 284 | 0.002 | 25 | 0.003 | 0.046 |
| sTNFsr1/ pMIP-1α | pre-op | 278 | 0.099 | 25 | 0.121 | 0.028 |
| sTNFsr1/ pMCP-1 | pre-op | 282 | 0.0028 | 25 | 0.0034 | 0.037 |
| sTNFsr1/ pNGAL | pre-op | 283 | 0.0006 | 25 | 0.0008 | 0.001 |
| sTNFsr1/ pNGAL | post-op | 282 | 0.0007 | 25 | 0.0009 | 0.014 |
| sTNFsr2/ pIL-6 | post-op | 280 | 0.006 | 25 | 0.012 | 0.015 |
| sTNFsr2/ sIL-12p40 | post-op | 284 | 0.003 | 25 | 0.004 | 0.011 |
| sTNFsr2/ pNGAL | pre-op | 283 | 0.0007 | 25 | 0.0009 | 0.015 |
| sTNFsr2/ pNGAL | post-op | 282 | 0.0008 | 25 | 0.0011 | 0.023 |
| sIL-1RA/ pIL-6 | post-op | 280 | 3.789 | 25 | 5.657 | 0.047 |
| sIL-1RA/ pNGAL | pre-op | 283 | 0.115 | 25 | 0.162 | 0.031 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, sIL-12p40 – serum interleukin 12 subunit p40, pMIP-1α – plasma macrophage inflammatory protein 1α, pMCP-1 – plasma monocyte chemotactic protein 1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin 1 receptor antagonist

Supplemental Table 8. Ratios of urinary anti-inflammatory/urinary pro-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ urinary pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uIL-1RA/ uIP-10 | post-op | 266 | 0.408 | 25 | 0.268 | 0.013 |
| uIL-1RA/ uNGAL | post-op | 274 | 0.045 | 25 | 0.037 | 0.017 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uIL-1RA – urinary interleukin-1 receptor antagonist, uIP-10 – urinary interferon gamma - induced protein-10, uNGAL – urinary neutrophil gelatinase-associated lipocalin

Supplemental Table 9. Ratios of urinary anti-inflammatory/blood pro-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uIL-1RA/ pTNFα | post-op | 242 | 712.086 | 23 | 556.637 | 0.014 |
| uIL-1RA/ pIL-6 | pre-op | 262 | 552.969 | 25 | 358.745 | 0.028 |
| uIL-1RA/ pIL-8 | post-op | 282 | 209.435 | 25 | 150.119 | 0.021 |
| uIL-1RA/ sIP-10 | post-op | 279 | 18.212 | 25 | 11.138 | 0.019 |
| uIL-1RA/ sIL-12p40 | post-op | 279 | 6.463 | 25 | 4.350 | 0.007 |
| uIL-1RA/ pMIP-1α | post-op | 278 | 389.484 | 25 | 218.909 | <0.001 |
| uIL-1RA/ pMCP-1 | post-op | 282 | 9.029 | 25 | 5.407 | 0.001 |
| uIL-1RA/ sMK | post-op | 237 | 1.774 | 21 | 0.955 | 0.026 |
| uIL-1RA/ pNGAL | post-op | 282 | 1.834 | 25 | 1.241 | 0.003 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uIL-1RA – urinary interleukin-1 receptor antagonist, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, sIP-10 – serum interferon gamma - induced protein-10, sIL-12p40 – serum interleukin 12 subunit p40, pMIP-1α – plasma macrophage inflammatory protein 1α, pMCP-1 – plasma monocyte chemotactic protein 1, sMK – serum midkine, pNGAL – plasma neutrophil gelatinase-associated lipocalin

Supplemental Table 10. Blood hypoperfusion biomarkers (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Serum biomarker** | | | | | | |
| sH-FABP | pre-op | 288 | 4.935 | 24 | 7.110 | 0.021 |
| sH-FABP | post-op | 287 | 19.500 | 25 | 46.780 | <0.001 |
| **Plasma biomarker** | | | | | | |
| pVEGF | pre-op | 283 | 31.000 | 25 | 37.000 | 0.022 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sH-FABP – serum heart-type fatty acid-binding protein, pVEGF – plasma vascular endothelial growth factor

Supplemental Table 11. Ratios of urinary anti-inflammatory/blood hypoperfusion biomarkers (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sH-FABP | post-op | 278 | 0.323 | 25 | 0.140 | 0.001 |
| uTNFsr2/ sH-FABP | post-op | 279 | 0.402 | 25 | 0.149 | 0.001 |
| uIL-1RA/ sH-FABP | post-op | 270 | 3.059 | 25 | 2.566 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sH-FABP – serum heart-type fatty acid-binding protein, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist

Supplemental Table 12. Ratios of blood anti-inflammatory/urinary anti-inflammatory cytokines (Day 1)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ urinary anti-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 1** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ uTNFsr1 | post-op | 277 | 0.109 | 25 | 0.136 | 0.029 |
| sTNFsr1/ uTNFsr2 | post-op | 278 | 0.088 | 25 | 0.121 | 0.021 |
| sTNFsr1/ uIL-1RA | pre-op | 285 | 0.0002 | 25 | 0.0003 | 0.026 |
| sTNFsr1/ uIL-1RA | post-op | 279 | 0.0004 | 25 | 0.0006 | <0.001 |
| sTNFsr2/ uTNFsr1 | post-op | 277 | 0.119 | 25 | 0.157 | 0.020 |
| sTNFsr2/ uTNFsr2 | post-op | 278 | 0.099 | 25 | 0.141 | 0.018 |
| sTNFsr2/ uIL-1RA | post-op | 279 | 0.0004 | 25 | 0.0007 | <0.001 |
| sIL-1RA/ uIL-1RA | post-op | 279 | 0.236 | 25 | 0.489 | 0.006 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist

Supplemental Table 13. Ratios of blood anti-inflammatory/blood pro-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ pTNFα | pre-op | 222 | 0.156 | 51 | 0.201 | 0.001 |
| sTNFsr1/ pTNFα | post-op | 226 | 0.266 | 52 | 0.327 | 0.002 |
| sTNFsr1/ pIL-6 | post-op | 265 | 0.006 | 56 | 0.007 | 0.010 |
| sTNFsr1/ pIL-8 | pre-op | 268 | 0.124 | 55 | 0.150 | 0.007 |
| sTNFsr1/ sIP-10 | pre-op | 275 | 0.003 | 55 | 0.004 | 0.008 |
| sTNFsr1/ pMIP-1α | pre-op | 265 | 0.098 | 54 | 0.127 | <0.001 |
| sTNFsr1/ pMCP-1 | pre-op | 268 | 0.003 | 55 | 0.004 | <0.001 |
| sTNFsr1/ pMCP-1 | post-op | 266 | 0.003 | 56 | 0.004 | 0.003 |
| sTNFsr1/ sMK | pre-op | 222 | 0.0006 | 50 | 0.0008 | 0.047 |
| sTNFsr1/ sMK | post-op | 221 | 0.0007 | 50 | 0.0005 | 0.033 |
| sTNFsr1/ pNGAL | pre-op | 269 | 0.0006 | 55 | 0.0008 | <0.001 |
| sTNFsr2/ pTNFα | pre-op | 222 | 0.154 | 51 | 0.211 | 0.002 |
| sTNFsr2/ pTNFα | post-op | 226 | 0.294 | 52 | 0.365 | 0.003 |
| sTNFsr2/ pIL-6 | post-op | 265 | 0.006 | 56 | 0.009 | 0.002 |
| sTNFsr2/ pIL-8 | pre-op | 268 | 0.118 | 55 | 0.168 | 0.004 |
| sTNFsr2/ pIL-8 | post-op | 266 | 0.082 | 56 | 0.101 | 0.038 |
| sTNFsr2/ sIP-10 | pre-op | 275 | 0.003 | 55 | 0.004 | 0.016 |
| sTNFsr2/ sIP-10 | post-op | 269 | 0.007 | 56 | 0.009 | 0.028 |
| sTNFsr2/ pMIP-1α | pre-op | 265 | 0.100 | 54 | 0.128 | 0.002 |
| sTNFsr2/ pMCP-1 | pre-op | 268 | 0.003 | 55 | 0.004 | <0.001 |
| sTNFsr2/ pMCP-1 | post-op | 266 | 0.004 | 56 | 0.005 | 0.001 |
| sTNFsr2/ sMK | pre-op | 222 | 0.0006 | 50 | 0.0010 | 0.008 |
| sTNFsr2/ pNGAL | pre-op | 269 | 0.0007 | 55 | 0.0009 | 0.001 |
| sIL-1RA/ pTNFα | post-op | 226 | 176.803 | 52 | 241.395 | 0.010 |
| sIL-1RA/ pIL-6 | post-op | 265 | 3.711 | 56 | 5.605 | 0.003 |
| sIL-1RA/ sIP-10 | post-op | 269 | 4.124 | 56 | 5.717 | 0.050 |
| sIL-1RA/ pMCP-1 | post-op | 266 | 2.111 | 56 | 3.036 | 0.009 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, sIP-10 – serum interferon gamma - induced protein-10, pMIP-1α – plasma macrophage inflammatory protein 1α, pMCP-1 – plasma monocyte chemotactic protein 1, sMK – serum midkine, pNGAL – plasma neutrophil gelatinase-associated lipocalin, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin 1 receptor antagonist

Supplemental Table 14. Ratios of urinary anti-inflammatory/urinary pro-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ urinary pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr2/ uIP-10 | post-op | 253 | 0.477 | 54 | 0.331 | 0.013 |
| uTNFsr2/ uNGAL | post-op | 261 | 0.052 | 55 | 0.040 | 0.008 |
| uIL-1RA/ uIP-10 | post-op | 253 | 121.742 | 54 | 87.261 | 0.013 |
| uIL-1RA/ uIL-12p40 | post-op | 180 | 504.560 | 48 | 350.832 | 0.005 |
| uIL-1RA/ uNGAL | post-op | 261 | 13.150 | 55 | 8.193 | 0.002 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIP-10 – urinary interferon gamma - induced protein-10, uNGAL – urinary neutrophil gelatinase-associated lipocalin, uIL-1RA – urinary interleukin-1 receptor antagonist, uIL-12p40 – urinary interleukin-12 subunit p40

Supplemental Table 15. Ratios of urinary anti-inflammatory/blood pro-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sIL-12p40 | post-op | 262 | 0.023 | 56 | 0.019 | 0.035 |
| uTNFsr1/ sMK | post-op | 216 | 0.006 | 50 | 0.003 | 0.002 |
| uTNFsr1/ pNGAL | post-op | 265 | 0.007 | 56 | 0.006 | 0.047 |
| uTNFsr2/ sIL-12p40 | post-op | 263 | 0.029 | 56 | 0.022 | 0.002 |
| uTNFsr2/ pMIP-1α | post-op | 262 | 1.633 | 56 | 1.448 | 0.044 |
| uTNFsr2/ sMK | post-op | 217 | 0.008 | 50 | 0.004 | <0.001 |
| uTNFsr2/ pNGAL | post-op | 266 | 0.008 | 56 | 0.006 | 0.003 |
| uIL-1RA/ pTNFα | post-op | 228 | 724.509 | 52 | 588.911 | 0.030 |
| uIL-1RA/ pIL-6 | pre-op | 248 | 570.518 | 55 | 419.013 | 0.030 |
| uIL-1RA/ pIL-8 | post-op | 267 | 208.048 | 56 | 163.944 | 0.020 |
| uIL-1RA/ sIL-12p40 | pre-op | 271 | 3.558 | 55 | 2.969 | 0.004 |
| uIL-1RA/ sIL-12p40 | post-op | 264 | 6.786 | 56 | 4.227 | <0.001 |
| uIL-1RA/ pMIP-1α | post-op | 263 | 398.101 | 56 | 284.401 | <0.001 |
| uIL-1RA/ pMCP-1 | post-op | 267 | 9.125 | 56 | 7.336 | 0.003 |
| uIL-1RA/ sMK | post-op | 218 | 1.876 | 50 | 0.772 | <0.001 |
| uIL-1RA/ pNGAL | pre-op | 265 | 2.606 | 55 | 2.063 | 0.023 |
| uIL-1RA/ pNGAL | post-op | 267 | 1.928 | 56 | 1.163 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sIL-12p40 – serum interleukin 12 subunit p40, sMK – serum midkine, pNGAL – plasma neutrophil gelatinase-associated lipocalin, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, pMIP-1α – plasma macrophage inflammatory protein 1α, uIL-1RA – urinary interleukin-1 receptor antagonist, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, pMCP-1 – plasma monocyte chemotactic protein 1

Supplemental Table 16. Blood hypoperfusion biomarkers (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Serum biomarker** | | | | | | |
| sH-FABP | pre-op | 274 | 4.880 | 54 | 6.430 | 0.004 |
| sH-FABP | post-op | 272 | 18.305 | 56 | 44.760 | <0.001 |
| **Plasma biomarker** | | | | | | |
| pVEGF | pre-op | 269 | 30.000 | 55 | 34.070 | 0.005 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sH-FABP – serum heart-type fatty acid-binding protein, pVEGF – plasma vascular endothelial growth factor

Supplemental Table 17. Ratios of urinary anti-inflammatory/blood hypoperfusion biomarkers (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sH-FABP | post-op | 263 | 0.323 | 56 | 0.156 | <0.001 |
| uTNFsr2/ sH-FABP | post-op | 264 | 0.434 | 56 | 0.182 | <0.001 |
| uIL-1RA/ sH-FABP | pre-op | 257 | 4.399 | 53 | 3.916 | 0.050 |
| uIL-1RA/ sH-FABP | post-op | 256 | 3.104 | 55 | 2.529 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sH-FABP – serum heart-type fatty acid-binding protein, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist

Supplemental Table 18. Ratios of blood anti-inflammatory/urinary anti-inflammatory cytokines (Day 2)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ urinary anti-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 2** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ uTNFsr1 | post-op | 262 | 0.108 | 56 | 0.123 | 0.044 |
| sTNFsr1/ uTNFsr2 | post-op | 263 | 0.087 | 56 | 0.117 | 0.003 |
| sTNFsr1/ uIL-1RA | pre-op | 271 | 0.0002 | 55 | 0.0003 | <0.001 |
| sTNFsr1/ uIL-1RA | post-op | 264 | 0.0004 | 56 | 0.0006 | <0.001 |
| sTNFsr2/ uTNFsr1 | post-op | 262 | 0.118 | 56 | 0.154 | 0.011 |
| sTNFsr2/ uTNFsr2 | post-op | 263 | 0.098 | 56 | 0.137 | <0.001 |
| sTNFsr2/ uIL-1RA | pre-op | 271 | 0.0002 | 55 | 0.0004 | <0.001 |
| sTNFsr2/ uIL-1RA | post-op | 264 | 0.0004 | 56 | 0.0007 | <0.001 |
| sIL-1RA/ uTNFsr2 | post-op | 263 | 56.157 | 56 | 87.080 | 0.011 |
| sIL-1RA/ uIL-1RA | post-op | 264 | 0.232 | 56 | 0.442 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist

Supplemental Table 19. Ratios of blood anti-inflammatory/blood pro-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ pTNFα | pre-op | 243 | 0.162 | 21 | 0.184 | 0.044 |
| sTNFsr1/ pIL-6 | post-op | 289 | 0.006 | 22 | 0.009 | 0.037 |
| sTNFsr1/ sIP-10 | pre-op | 298 | 0.003 | 22 | 0.004 | 0.021 |
| sTNFsr1/ pMIP-1α | pre-op | 287 | 0.101 | 22 | 0.129 | 0.011 |
| sTNFsr1/ pMCP-1 | pre-op | 291 | 0.003 | 22 | 0.004 | 0.002 |
| sTNFsr1/ pNGAL | pre-op | 292 | 0.0006 | 22 | 0.0008 | 0.061 |
| sTNFsr2/ pTNFα | pre-op | 243 | 0.167 | 21 | 0.225 | 0.012 |
| sTNFsr2/ pIL-6 | post-op | 289 | 0.006 | 22 | 0.010 | 0.039 |
| sTNFsr2/ pIL-8 | pre-op | 291 | 0.127 | 22 | 0.182 | 0.028 |
| sTNFsr2/ sIP-10 | pre-op | 298 | 0.003 | 22 | 0.005 | 0.019 |
| sTNFsr2/ pMIP-1α | pre-op | 287 | 0.106 | 22 | 0.177 | 0.008 |
| sTNFsr2/ pMCP-1 | pre-op | 291 | 0.003 | 22 | 0.004 | 0.003 |
| sTNFsr2/ pNGAL | pre-op | 292 | 0.0007 | 22 | 0.0009 | 0.039 |
| sIL-1RA/ pTNFα | post-op | 247 | 174.979 | 21 | 321.413 | 0.009 |
| sIL-1RA/ pIL-6 | post-op | 289 | 3.853 | 22 | 6.738 | 0.004 |
| sIL-1RA/ pMCP-1 | post-op | 290 | 2.122 | 22 | 3.414 | 0.016 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, sIP-10 – serum interferon gamma - induced protein-10, pMIP-1α – plasma macrophage inflammatory protein 1α, pMCP-1 – plasma monocyte chemotactic protein 1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, pIL-8 – plasma interleukin 8, sIL-1RA – serum interleukin 1 receptor antagonist, sMK – serum midkine

Supplemental Table 20. Ratios of urinary anti-inflammatory/urinary pro-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ urinary pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ uIL-12p40 | post-op | 203 | 1.566 | 17 | 0.930 | 0.029 |
| uTNFsr2/ uIP-10 | post-op | 276 | 0.460 | 21 | 0.372 | 0.041 |
| uTNFsr2/ uIL-12p40 | post-op | 203 | 1.863 | 17 | 1.211 | 0.033 |
| uTNFsr2/ uNGAL | post-op | 285 | 0.052 | 21 | 0.040 | 0.036 |
| uIL-1RA/ uIP-10 | post-op | 276 | 125.720 | 21 | 69.580 | 0.017 |
| uIL-1RA/ uIL-12p40 | post-op | 204 | 480.156 | 17 | 338.779 | 0.019 |
| uIL-1RA/ uNGAL | post-op | 285 | 12.685 | 21 | 7.803 | 0.010 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uIL-12p40 – urinary interleukin-12 subunit p40, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIP-10 – urinary interferon gamma - induced protein-10, uNGAL – urinary neutrophil gelatinase-associated lipocalin, uIL-1RA – urinary interleukin-1 receptor antagonist

Supplemental Table 21. Ratios of urinary anti-inflammatory/blood pro-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr2/ pIL-8 | post-op | 290 | 0.854 | 22 | 0.606 | 0.037 |
| uTNFsr2/ sIL-12p40 | post-op | 287 | 0.029 | 22 | 0.021 | 0.019 |
| uTNFsr2/ pMIP-1α | post-op | 286 | 1.633 | 22 | 1.229 | 0.014 |
| uTNFsr2/ sMK | post-op | 241 | 0.007 | 18 | 0.003 | 0.033 |
| uTNFsr2/ pNGAL | post-op | 290 | 0.008 | 22 | 0.006 | 0.007 |
| uIL-1RA/ pTNFα | post-op | 249 | 704.104 | 21 | 543.804 | 0.024 |
| uIL-1RA/ pIL-6 | pre-op | 271 | 554.184 | 22 | 361.242 | 0.039 |
| uIL-1RA/ pIL-8 | post-op | 291 | 208.970 | 22 | 123.796 | 0.010 |
| uIL-1RA/ sIL-12p40 | pre-op | 294 | 3.537 | 22 | 1.851 | 0.001 |
| uIL-1RA/ sIL-12p40 | post-op | 288 | 6.381 | 22 | 3.938 | 0.002 |
| uIL-1RA/ pMIP-1α | pre-op | 283 | 427.891 | 22 | 343.930 | 0.032 |
| uIL-1RA/ pMIP-1α | post-op | 287 | 384.318 | 22 | 252.012 | <0.001 |
| uIL-1RA/ pMCP-1 | post-op | 291 | 9.029 | 22 | 5.890 | 0.015 |
| uIL-1RA/ sMK | post-op | 242 | 1.766 | 18 | 0.718 | 0.008 |
| uIL-1RA/ pNGAL | pre-op | 288 | 2.616 | 22 | 1.593 | 0.017 |
| uIL-1RA/ pNGAL | post-op | 291 | 1.840 | 22 | 1.110 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, pIL-8 – plasma interleukin 8, sIL-12p40 – serum interleukin 12 subunit p40, pMIP-1α – plasma macrophage inflammatory protein 1α, sMK – serum midkine, pNGAL – plasma neutrophil gelatinase-associated lipocalin, uIL-1RA – urinary interleukin-1 receptor antagonist, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, pMCP-1 – plasma monocyte chemotactic protein 1

Supplemental Table 22. Blood hypoperfusion biomarkers (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Serum biomarker** | | | | | | |
| sH-FABP | post-op | 296 | 19.885 | 22 | 38.735 | 0.002 |
| **Plasma biomarker** | | | | | | |
| pVEGF | pre-op | 292 | 30.500 | 22 | 46.190 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sH-FABP – serum heart-type fatty acid-binding protein, pVEGF – plasma vascular endothelial growth factor

Supplemental Table 23. Ratios of urinary anti-inflammatory/blood hypoperfusion biomarkers (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sH-FABP | post-op | 287 | 0.317 | 22 | 0.169 | 0.017 |
| uTNFsr2/ sH-FABP | post-op | 288 | 0.399 | 22 | 0.196 | 0.005 |
| uIL-1RA/ sH-FABP | post-op | 280 | 3.025 | 21 | 2.514 | 0.006 |
| uIL-1RA/ pVEGF | pre-op | 265 | 49.380 | 22 | 32.530 | 0.008 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sH-FABP – serum heart-type fatty acid-binding protein, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist

Supplemental Table 24. Ratios of blood anti-inflammatory/urinary anti-inflammatory cytokines (Day 5)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ urinary anti-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Day 5** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ uTNFsr1 | pre-op | 293 | 0.675 | 22 | 1.009 | 0.050 |
| sTNFsr1/ uTNFsr1 | post-op | 286 | 0.109 | 22 | 0.159 | 0.021 |
| sTNFsr1/ uTNFsr2 | pre-op | 281 | 0.371 | 22 | 0.667 | 0.050 |
| sTNFsr1/ uTNFsr2 | post-op | 287 | 0.088 | 22 | 0.128 | 0.001 |
| sTNFsr1/ uIL-1RA | pre-op | 294 | 0.0002 | 22 | 0.0004 | 0.002 |
| sTNFsr1/ uIL-1RA | post-op | 288 | 0.0004 | 22 | 0.0006 | <0.001 |
| sTNFsr2/ uTNFsr1 | pre-op | 293 | 0.684 | 22 | 1.034 | 0.050 |
| sTNFsr2/ uTNFsr1 | post-op | 286 | 0.121 | 22 | 0.180 | 0.028 |
| sTNFsr2/ uTNFsr2 | pre-op | 281 | 0.431 | 22 | 0.547 | 0.050 |
| sTNFsr2/ uTNFsr2 | post-op | 287 | 0.099 | 22 | 0.135 | 0.003 |
| sTNFsr2/ uIL-1RA | pre-op | 294 | 0.0003 | 22 | 0.0005 | 0.004 |
| sTNFsr2/ uIL-1RA | post-op | 288 | 0.0004 | 22 | 0.0007 | <0.001 |
| sIL-1RA/ uTNFsr1 | post-op | 286 | 68.847 | 22 | 149.826 | 0.014 |
| sIL-1RA/ uTNFsr2 | post-op | 287 | 56.775 | 22 | 120.819 | 0.003 |
| sIL-1RA/ uIL-1RA | post-op | 288 | 0.237 | 22 | 0.653 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist

Supplemental Table 25. Ratios of blood anti-inflammatory/blood pro-inflammatory cytokines (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ pTNFα | pre-op | 208 | 0.156 | 59 | 0.195 | <0.001 |
| sTNFsr1/ pTNFα | post-op | 211 | 0.264 | 61 | 0.329 | <0.001 |
| sTNFsr1/ pIL-6 | post-op | 250 | 0.006 | 65 | 0.007 | 0.036 |
| sTNFsr1/ pIL-8 | pre-op | 253 | 0.124 | 64 | 0.144 | 0.032 |
| sTNFsr1/ sIP-10 | pre-op | 260 | 0.003 | 64 | 0.004 | 0.013 |
| sTNFsr1/ pMIP-1α | pre-op | 250 | 0.098 | 63 | 0.121 | 0.001 |
| sTNFsr1/ pMCP-1 | pre-op | 253 | 0.003 | 64 | 0.004 | <0.001 |
| sTNFsr1/ pMCP-1 | post-op | 251 | 0.003 | 65 | 0.004 | 0.003 |
| sTNFsr1/ pNGAL | pre-op | 254 | 0.0006 | 64 | 0.0008 | <0.001 |
| sTNFsr2/ pTNFα | pre-op | 208 | 0.150 | 59 | 0.215 | <0.001 |
| sTNFsr2/ pTNFα | post-op | 211 | 0.290 | 61 | 0.368 | <0.001 |
| sTNFsr2/ pIL-6 | post-op | 250 | 0.006 | 65 | 0.009 | 0.005 |
| sTNFsr2/ pIL-8 | pre-op | 253 | 0.115 | 64 | 0.172 | 0.003 |
| sTNFsr2/ pIL-8 | post-op | 251 | 0.081 | 65 | 0.100 | 0.045 |
| sTNFsr2/ sIP-10 | pre-op | 260 | 0.003 | 64 | 0.004 | 0.011 |
| sTNFsr2/ sIP-10 | post-op | 254 | 0.007 | 65 | 0.009 | 0.016 |
| sTNFsr2/ pMIP-1α | pre-op | 250 | 0.100 | 63 | 0.130 | 0.001 |
| sTNFsr2/ pMCP-1 | pre-op | 253 | 0.003 | 64 | 0.004 | <0.001 |
| sTNFsr2/ pMCP-1 | post-op | 251 | 0.004 | 65 | 0.005 | <0.001 |
| sTNFsr2/ sMK | pre-op | 210 | 0.0006 | 58 | 0.0009 | 0.008 |
| sTNFsr2/ pNGAL | pre-op | 254 | 0.0007 | 64 | 0.0009 | <0.001 |
| sIL-1RA/ pTNFα | post-op | 211 | 174.510 | 61 | 276.730 | 0.001 |
| sIL-1RA/ pIL-6 | post-op | 250 | 3.746 | 65 | 5.553 | 0.004 |
| sIL-1RA/ pIL-8 | post-op | 251 | 47.448 | 65 | 64.913 | 0.026 |
| sIL-1RA/ sIP-10 | post-op | 254 | 4.088 | 65 | 6.397 | 0.014 |
| sIL-1RA/ pMCP-1 | post-op | 251 | 2.053 | 65 | 3.186 | 0.001 |
| sIL-1RA/ pNGAL | post op | 252 | 0.446 | 65 | 0.715 | 0.035 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, sIP-10 – serum interferon gamma - induced protein-10, pMIP-1α – plasma macrophage inflammatory protein 1α, pMCP-1 – plasma monocyte chemotactic protein 1, pNGAL – plasma neutrophil gelatinase-associated lipocalin, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sMK – serum midkine, sIL-1RA – serum interleukin 1 receptor antagonist

Supplemental Table 26. Ratios of urinary anti-inflammatory/urinary pro-inflammatory cytokines (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ urinary pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ uIP-10 | post-op | 237 | 0.410 | 63 | 0.314 | 0.048 |
| uTNFsr1/ uNGAL | post-op | 245 | 0.044 | 64 | 0.037 | 0.049 |
| uTNFsr2/ uIP-10 | post-op | 238 | 0.478 | 63 | 0.335 | 0.004 |
| uTNFsr2/ uNGAL | post-op | 246 | 0.053 | 64 | 0.040 | 0.004 |
| uIL-1RA/ uIP-10 | post-op | 238 | 127.555 | 63 | 81.196 | 0.001 |
| uIL-1RA/ uIL-12p40 | post-op | 169 | 512.772 | 54 | 350.832 | 0.001 |
| uIL-1RA/ uNGAL | post-op | 246 | 13.551 | 64 | 8.051 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uIP-10 – urinary interferon gamma - induced protein-10, uNGAL – urinary neutrophil gelatinase-associated lipocalin, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist, uIL-12p40 – urinary interleukin-12 subunit p40

Supplemental Table 27. Ratios of urinary anti-inflammatory/blood pro-inflammatory cytokines (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood pro-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sIL-12p40 | post-op | 247 | 0.023 | 65 | 0.019 | 0.015 |
| uTNFsr1/ sMK | post-op | 204 | 0.006 | 58 | 0.003 | 0.003 |
| uTNFsr2/ sIL-12p40 | post-op | 248 | 0.030 | 65 | 0.022 | 0.001 |
| uTNFsr2/ pMIP-1α | post-op | 247 | 1.638 | 65 | 1.421 | 0.026 |
| uTNFsr2/ sMK | post-op | 205 | 0.008 | 58 | 0.004 | <0.001 |
| uTNFsr2/ pNGAL | post-op | 251 | 0.008 | 65 | 0.006 | 0.007 |
| uIL-1RA/ pTNFα | post-op | 213 | 725.734 | 61 | 586.286 | 0.002 |
| uIL-1RA/ pIL-6 | pre-op | 233 | 583.157 | 64 | 382.638 | 0.004 |
| uIL-1RA/ pIL-6 | post-op | 251 | 16.614 | 65 | 12.810 | 0.028 |
| uIL-1RA/ pIL-8 | post-op | 252 | 214.216 | 65 | 157.119 | 0.030 |
| uIL-1RA/ sIP-10 | post-op | 249 | 17.685 | 65 | 14.805 | 0.039 |
| uIL-1RA/ sIL-12p40 | pre-op | 256 | 3.588 | 64 | 2.856 | <0.001 |
| uIL-1RA/ sIL-12p40 | post-op | 249 | 7.080 | 65 | 4.197 | <0.001 |
| uIL-1RA/ pMIP-1α | pre-op | 246 | 439.349 | 63 | 367.121 | 0.014 |
| uIL-1RA/ pMIP-1α | post-op | 248 | 421.239 | 65 | 263.916 | <0.001 |
| uIL-1RA/ pMCP-1 | post-op | 252 | 9.228 | 65 | 7.067 | <0.001 |
| uIL-1RA/ sMK | post-op | 206 | 1.917 | 58 | 0.789 | <0.001 |
| uIL-1RA/ pNGAL | pre-op | 250 | 2.634 | 64 | 2.057 | 0.011 |
| uIL-1RA/ pNGAL | post-op | 252 | 1.951 | 65 | 1.214 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sIL-12p40 – serum interleukin-12 subunit p40, sMK – serum midkine, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, pMIP-1α – plasma macrophage inflammatory protein 1α, pNGAL – plasma neutrophil gelatinase-associated lipocalin, uIL-1RA – urinary interleukin-1 receptor antagonist, pTNFα – plasma tumour necrosis factor α, pIL-6 – plasma interleukin-6, pIL-8 – plasma interleukin 8, sIP-10 – serum interferon gamma - induced protein-10, pMCP-1 – plasma monocyte chemotactic protein 1

Supplemental Table 28. Blood hypoperfusion biomarkers (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **median** | **n** | **median** |
| **Serum biomarker** | | | | | | |
| sH-FABP | pre-op | 259 | 4.810 | 63 | 6.530 | 0.001 |
| sH-FABP | post-op | 257 | 17.160 | 65 | 43.220 | <0.001 |
| **Plasma biomarker** | | | | | | |
| pVEGF | pre-op | 254 | 30.000 | 64 | 35.000 | 0.002 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sH-FABP – serum heart-type fatty acid-binding protein, pVEGF – plasma vascular endothelial growth factor

Supplemental Table 29. Ratios of urinary anti-inflammatory/blood hypoperfusion biomarkers (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Urinary anti-inflammatory/ blood hypoperfusion biomarkers** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| uTNFsr1/ sH-FABP | post-op | 248 | 0.329 | 65 | 0.168 | <0.001 |
| uTNFsr2/ sH-FABP | post-op | 249 | 0.439 | 65 | 0.196 | <0.001 |
| uIL-1RA/ sH-FABP | pre-op | 242 | 4.454 | 62 | 3.923 | 0.023 |
| uIL-1RA/ sH-FABP | post-op | 241 | 3.146 | 64 | 2.547 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, sH-FABP – serum heart-type fatty acid-binding protein, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist

Supplemental Table 30. Ratios of blood anti-inflammatory/urinary anti-inflammatory cytokines (Any day)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Blood anti-inflammatory/ urinary anti-inflammatory cytokines** | **Pre-op**  **or**  **post-op** | **Any day** | | | | |
| **non-CS-AKI** | | **CS-AKI** | | **p value** |
| **n** | **ratio** | **n** | **ratio** |
| sTNFsr1/ uTNFsr1 | post-op | 247 | 0.108 | 65 | 0.118 | 0.028 |
| sTNFsr1/ uTNFsr2 | post-op | 248 | 0.087 | 65 | 0.117 | 0.002 |
| sTNFsr1/ uIL-1RA | pre-op | 256 | 0.0002 | 64 | 0.0003 | <0.001 |
| sTNFsr1/ uIL-1RA | post-op | 249 | 0.0004 | 65 | 0.0006 | <0.001 |
| sTNFsr2/ uTNFsr1 | pre-op | 255 | 0.676 | 64 | 0.997 | 0.044 |
| sTNFsr2/ uTNFsr1 | post-op | 247 | 0.117 | 65 | 0.157 | 0.004 |
| sTNFsr2/ uTNFsr2 | post-op | 248 | 0.096 | 65 | 0.136 | <0.001 |
| sTNFsr2/ uIL-1RA | pre-op | 256 | 0.0002 | 64 | 0.0004 | <0.001 |
| sTNFsr2/ uIL-1RA | post-op | 249 | 0.0004 | 65 | 0.0007 | <0.001 |
| sIL-1RA/ uTNFsr1 | post-op | 247 | 67.434 | 65 | 93.093 | 0.016 |
| sIL-1RA/ uTNFsr2 | post-op | 248 | 55.121 | 65 | 98.477 | 0.002 |
| sIL-1RA/ uIL-1RA | pre-op | 256 | 0.045 | 64 | 0.054 | 0.015 |
| sIL-1RA/ uIL-1RA | post-op | 249 | 0.224 | 65 | 0.468 | <0.001 |

pre-op – preoperative, post-op – postoperative, CS-AKI – cardiac surgery acute kidney injury, n – number of patients, sTNFsr1 – serum tumour necrosis factor soluble receptor 1, uTNFsr1 – urinary tumour necrosis factor soluble receptor 1, uTNFsr2 – urinary tumour necrosis factor soluble receptor 2, uIL-1RA – urinary interleukin-1 receptor antagonist, sTNFsr2 – serum tumour necrosis factor soluble receptor 2, sIL-1RA – serum interleukin-1 receptor antagonist