

Supplementary File 1: Biomarker levels in the cardiac and orthopaedic cohorts pre- and post-operatively.

		All Patients				Non-AKI Patients				AKI Patients					
Marker Type	Biomarker	Cardiac [mean±SD]	Fracture [mean±SD]	p value	Change	Cardiac [mean±SD]	Fracture [mean±SD]	p value	Change	Cardiac [mean±SD]	Fracture [mean±SD]	p value	Change		
Preoperative	Blood anti-inflammatory	sTNFR1 (Serum)	0.487 ± 0.759 (n=324)	0.799 ± 0.345 (n=174)	<0.001	Fracture ↑	0.455 ± 0.821 (n=260)	0.719 ± 0.312 (n=119)	<0.001	Fracture ↑	0.619 ± 0.395 (n=64)	0.972 ± 0.352 (n=55)	<0.001	Fracture ↑	
	Blood anti-inflammatory	sTNFR2 (Serum)	0.517 ± 0.477 (n=324)	0.987 ± 0.797 (n=174)	<0.001	Fracture ↑	0.448 ± 0.347 (n=260)	0.895 ± 0.777 (n=119)	<0.001	Fracture ↑	0.798 ± 0.757 (n=64)	1.185 ± 0.810 (n=55)	<0.001	Fracture ↑	
	Blood anti-inflammatory	IL-1Ra (Serum)	122.982 ± 225.601 (n=324)	347.906 ± 413.527 (n=175)	<0.001	Fracture ↑	107.465 ± 186.869 (n=260)	352.060 ± 433.609 (n=120)	<0.001	Fracture ↑	186.0180 ± 335.189 (n=64)	338.842 ± 369.539 (n=55)	<0.001	Fracture ↑	
	Blood anti-inflammatory	IL-10 (Plasma)	1.810 ± 5.862 (n=318)	3.210 ± 7.634 (n=184)	<0.001	Fracture ↑	1.645 ± 5.466 (n=254)	2.625 ± 4.696 (n=125)	<0.001	Fracture ↑	2.466 ± 7.234 (n=64)	4.451 ± 11.595 (n=59)	<0.001	Fracture ↑	
	Blood hypoperfusion	H-FABP (Serum)	9.403 ± 34.507 (n=322)	14.656 ± 15.555 (n=183)	<0.001	Fracture ↑	9.644 ± 38.364 (n=259)	12.700 ± 13.012 (n=125)	<0.001	Fracture ↑	8.408 ± 6.257 (n=63)	18.872 ± 19.436 (n=58)	<0.001	Fracture ↑	
	Blood hypoperfusion	VEGF (Plasma)	35.299 ± 23.448 (n=318)	54.612 ± 48.520 (n=184)	<0.001	Fracture ↑	33.216 ± 21.143 (n=254)	55.152 ± 53.677 (n=125)	<0.001	Fracture ↑	43.570 ± 29.738 (n=64)	53.469 ± 35.581 (n=59)	0.029	Fracture ↑	
	Blood pro-inflammatory	IL-6 (Plasma)	8.530 ± 41.424 (n=318)	76.471 ± 121.440 (n=184)	<0.001	Fracture ↑	9.035 ± 46.145 (n=254)	77.165 ± 134.952 (n=125)	<0.001	Fracture ↑	6.525 ± 8.840 (n=64)	75.001 ± 87.130 (n=59)	0.001	Fracture ↑	
	Blood pro-inflammatory	IL-8 (Plasma)	4.387 ± 5.770 (n=318)	12.780 ± 36.708 (n=184)	<0.001	Fracture ↑	4.234 ± 5.729 (n=254)	13.735 ± 42.301 (n=125)	<0.001	Fracture ↑	4.998 ± 5.936 (n=64)	10.754 ± 20.489 (n=59)	<0.001	Fracture ↑	
	Blood pro-inflammatory	TNFα (Plasma)	2.731 ± 7.947 (n=318)	4.011 ± 6.090 (n=184)	<0.001	Fracture ↑	2.729 ± 8.855 (n=254)	3.925 ± 7.085 (n=125)	<0.001	Fracture ↑	2.741 ± 1.691 (n=64)	4.195 ± 3.108 (n=59)	<0.001	Fracture ↑	
	Blood pro-inflammatory	MCP-1 (Plasma)	137.407 ± 50.517 (n=318)	204.594 ± 124.028 (n=184)	<0.001	Fracture ↑	133.985 ± 50.687 (n=254)	187.968 ± 89.065 (n=125)	<0.001	Fracture ↑	150.984 ± 47.843 (n=64)	239.820 ± 172.391 (n=59)	<0.001	Fracture ↑	
	Blood pro-inflammatory	MIP-1α (Plasma)	6.315 ± 30.653 (n=315)	6.293 ± 6.312 (n=184)	<0.001	Cardiac ↓	4.930 ± 17.302 (n=251)	5.473 ± 3.161 (n=125)	<0.001	Fracture ↑	11.748 ± 58.801 (n=64)	8.032 ± 9.990 (n=59)	<0.001	Cardiac ↓	
	Blood pro-inflammatory	NGAL (Plasma)	658.558 ± 309.175 (n=319)	909.768 ± 441.739 (n=184)	<0.001	Fracture ↑	631.144 ± 289.974 (n=255)	802.965 ± 421.030 (n=125)	<0.001	Fracture ↑	767.785 ± 358.226 (n=64)	1136.045 ± 400.037 (n=59)	<0.001	Fracture ↑	
	Blood pro-inflammatory	IL-12p40 (Serum)	476.312 ± 255.968 (n=324)	436.884 ± 262.204 (n=175)	0.076	Cardiac ↓	444.303 ± 240.381 (n=260)	399.778 ± 249.068 (n=120)	0.059	Cardiac ↓	606.351 ± 277.416 (n=64)	517.844 ± 274.023 (n=55)	0.072	Cardiac ↓	
	Blood pro-inflammatory	IP-10 (Serum)	144.508 ± 107.109 (n=324)	142.181 ± 117.243 (n=175)	0.335	Cardiac ↓	140.366 ± 110.830 (n=260)	138.983 ± 125.976 (n=120)	0.294	Cardiac ↓	161.335 ± 88.714 (n=64)	149.159 ± 96.162 (n=55)	0.312	Cardiac ↓	
	Blood pro-inflammatory	sIL2Rα (Serum)	0.195 ± 0.223 (n=324)	0.260 ± 0.363 (n=174)	<0.001	Fracture ↑	0.197 ± 0.242 (n=260)	0.261 ± 0.415 (n=119)	0.004	Fracture ↑	0.188 ± 0.119 (n=64)	0.259 ± 0.213 (n=55)	0.073	Fracture ↑	
	Blood pro-inflammatory	IL-2 (Plasma)	1.120 ± 5.133 (n=318)	2.153 ± 10.008 (n=184)	0.785	Fracture ↑	1.021 ± 5.257 (n=254)	2.556 ± 11.318 (n=125)	0.225	Fracture ↑	1.513 ± 4.623 (n=64)	1.297 ± 6.408 (n=59)	0.143	Cardiac ↓	
	Blood pro-inflammatory	IL-4 (Plasma)	0.467 ± 2.705 (n=318)	0.612 ± 2.229 (n=184)	0.563	Fracture ↑	0.486 ± 2.983 (n=254)	0.663 ± 2.605 (n=125)	0.874	Fracture ↑	0.391 ± 1.038 (n=64)	0.502 ± 1.070 (n=59)	0.313	Fracture ↑	
	Blood pro-inflammatory	IL-1α (Plasma)	0.188 ± 0.480 (n=318)	0.557 ± 2.024 (n=184)	0.431	Fracture ↑	0.163 ± 0.438 (n=254)	0.640 ± 2.290 (n=125)	0.233	Fracture ↑	0.285 ± 0.614 (n=64)	0.381 ± 1.295 (n=59)	0.436	Fracture ↑	
	Blood pro-inflammatory	IL-1β (Plasma)	0.776 ± 2.967 (n=318)	1.212 ± 4.884 (n=184)	0.721	Fracture ↑	0.744 ± 3.151 (n=254)	1.372 ± 5.477 (n=125)	0.746	Fracture ↑	0.902 ± 2.100 (n=64)	0.872 ± 3.312 (n=59)	0.640	Cardiac ↓	
	Blood pro-inflammatory	IFNγ (Plasma)	0.543 ± 2.119 (n=318)	1.274 ± 5.447 (n=184)	0.827	Fracture ↑	0.405 ± 1.659 (n=254)	1.358 ± 5.812 (n=125)	0.476	Fracture ↑	1.090 ± 3.341 (n=64)	1.097 ± 4.622 (n=59)	0.312	Fracture ↑	
	Blood pro-inflammatory	GM-CSF (Plasma)	1.551 ± 14.703 (n=315)	0.858 ± 1.752 (n=184)	0.407	Cardiac ↓	0.701 ± 0.619 (n=251)	0.748 ± 0.877 (n=125)	0.591	Fracture ↑	4.886 ± 32.584 (n=64)	1.090 ± 2.820 (n=59)	0.562	Cardiac ↓	
	Blood pro-inflammatory	sIL6R (Serum)	1.834 ± 1.034 (n=324)	2.259 ± 1.664 (n=174)	0.007	Fracture ↑	1.776 ± 0.982 (n=260)	2.137 ± 1.300 (n=119)	0.017	Fracture ↑	2.071 ± 1.201 (n=64)	2.521 ± 2.251 (n=59)	0.441	Fracture ↑	
	Blood pro-inflammatory	MMP9 (Serum)	18.352 ± 23.015 (n=324)	58.657 ± 56.136 (n=174)	<0.001	Fracture ↑	19.214 ± 23.551 (n=260)	61.138 ± 60.581 (n=119)	<0.001	Fracture ↑	14.850 ± 20.497 (n=64)	53.288 ± 45.090 (n=55)	<0.001	Fracture ↑	
	Blood IRI	Midkine (Serum)	1153.256 ± 1449.082 (n=269)	2265.953 ± 2144.934 (n=128)	<0.001	Fracture ↑	1138.945 ± 1475.047 (n=211)	2093.636 ± 2199.370 (n=86)	<0.001	Fracture ↑	1205.318 ± 1361.408 (n=58)	2618.793 ± 2008.198 (n=42)	<0.001	Fracture ↑	
	Urine IRI	Midkine (Urine)	329.353 ± 651.104 (n=279)	1897.309 ± 2055.507 (n=141)	<0.001	Fracture ↑	302.916 ± 623.745 (n=221)	1598.460 ± 2057.991 (n=93)	<0.001	Fracture ↑	430.085 ± 743.611 (n=58)	2476.329 ± 1945.028 (n=48)	<0.001	Fracture ↑	
	Urine anti-inflammatory	IL-1Ra (Urine)	2570.767 ± 4569.763 (n=310)	4642.025 ± 6637.355 (n=162)	<0.001	Fracture ↑	2360.301 ± 4118.766 (n=246)	5087.634 ± 7327.835 (n=110)	<0.001	Fracture ↑	3379.744 ± 5967.832 (n=64)	3699.390 ± 4793.242 (n=52)	0.263	Fracture ↑	
	Urine anti-inflammatory	sTNFR1 (Urine)	0.781 ± 0.841 (n=322)	3.142 ± 3.048 (n=171)	<0.001	Fracture ↑	0.760 ± 0.859 (n=257)	3.034 ± 3.350 (n=119)	<0.001	Fracture ↑	0.862 ± 0.766 (n=65)	3.391 ± 2.215 (n=52)	<0.001	Fracture ↑	
	Urine anti-inflammatory	sTNFR2 (Urine)	1.322 ± 1.556 (n=322)	4.579 ± 3.781 (n=170)	<0.001	Fracture ↑	1.258 ± 1.560 (n=257)	4.484 ± 4.090 (n=119)	<0.001	Fracture ↑	1.574 ± 1.526 (n=65)	4.802 ± 2.962 (n=51)	<0.001	Fracture ↑	
	Urine pro-inflammatory	NGAL (Urine)	110.474 ± 183.431 (n=310)	324.152 ± 350.299 (n=162)	<0.001	Fracture ↑	106.461 ± 182.443 (n=246)	318.949 ± 341.539 (n=110)	<0.001	Fracture ↑	125.902 ± 187.834 (n=64)	335.157 ± 371.330 (n=52)	<0.001	Fracture ↑	
	Urine pro-inflammatory	IL-12p40 (Urine)	7.606 ± 45.919 (n=323)	6.271 ± 10.314 (n=171)	<0.001	Cardiac ↓	4.991 ± 37.153 (n=258)	5.815 ± 8.400 (n=119)	<0.001	Fracture ↑	17.885 ± 70.207 (n=65)	7.315 ± 13.776 (n=52)	0.008	Cardiac ↓	
	Urine pro-inflammatory	IP-10 (Urine)	19.217 ± 47.639 (n=323)	50.332 ± 135.946 (n=170)	<0.001	Fracture ↑	18.445 ± 47.779 (n=258)	61.395 ± 158.784 (n=119)	<0.001	Fracture ↑	22.282 ± 47.320 (n=65)	24.519 ± 44.659 (n=51)	0.558	Fracture ↑	
	Urine pro-inflammatory	sIL2Rα (Urine)	0.079 ± 0.069 (n=322)	0.097 ± 0.069 (n=170)	<0.001	Fracture ↑	0.078 ± 0.070 (n=257)	0.102 ± 0.071 (n=118)	0.005	Fracture ↑	0.081 ± 0.064 (n=65)	0.086 ± 0.064 (n=52)	0.738	Fracture ↑	
	Urine pro-inflammatory	sIL6R (Urine)	0.134 ± 0.171 (n=322)	0.133 ± 0.116 (n=171)	0.805	Cardiac ↓	0.122 ± 0.131 (n=257)	0.132 ± 0.118 (n=119)	0.622	Fracture ↑	0.180 ± 0.274 (n=65)	0.136 ± 0.111 (n=52)	0.566	Cardiac ↓	
	Urine pro-inflammatory	MMP9 (Urine)	8.264 ± 51.839 (n=322)	18.043 ± 37.955 (n=170)	<0.001	Fracture ↑	8.945 ± 57.797 (n=257)	21.052 ± 43.999 (n=119)	<0.001	Fracture ↑	5.568 ± 10.356 (n=65)	11.021 ± 15.116 (n=51)	<0.001	Fracture ↑	
	Postoperative	Blood anti-inflammatory	sTNFR1 (Serum)	1.002 ± 2.483 (n=319)	1.077 ± 0.453 (n=147)	<0.001	Fracture ↑	0.968 ± 2.770 (n=254)	0.942 ± 0.391 (n=101)	<0.001	Cardiac ↓	1.137 ± 0.527 (n=65)	1.373 ± 0.444 (n=46)	0.002	Fracture ↑
		Blood anti-inflammatory	sTNFR2 (Serum)	0.928 ± 0.589 (n=319)	1.330 ± 0.866 (n=147)	<0.001	Fracture ↑	0.817 ± 0.492 (n=254)	1.127 ± 0.785 (n=101)	<0.001	Fracture ↑	1.359 ± 0.728 (n=65)	1.774 ± 0.878 (n=46)	0.005	Fracture ↑
		Blood anti-inflammatory	IL-1Ra (Serum)	667.057 ± 555.854 (n=319)	589.517 ± 491.079 (n=148)	0.222	Cardiac ↓	583.482 ± 491.670 (n=254)	505.450 ± 425.127 (n=102)	0.159	Cardiac ↓	993.643 ± 665.987 (n=65)	775.928 ± 574.978 (n=46)	0.110	Cardiac ↓
		Blood anti-inflammatory	IL-10 (Plasma)	5.849 ± 11.031 (n=324)	4.834 ± 17.601 (n=158)	<0.001	Cardiac ↓	5.674 ± 11.409 (n=259)	3.781 ± 9.847 (n=106)	0.001	Cardiac ↓	6.549 ± 9.422 (n=65)	6.979 ± 27.332 (n=52)	0.001	Fracture ↑
		Blood hypoperfusion	H-FABP (Serum)	38.712 ± 54.220 (n=322)	32.278 ± 25.446 (n=156)	0.217	Cardiac ↓	32.305 ± 46.865 (n=257)	23.558 ± 16.980 (n=108)	0.998	Cardiac ↓	64.045 ± 71.716 (n=65)	51.897 ± 30.185 (n=48)	0.632	Cardiac ↓
		Blood hypoperfusion	VEGF (Plasma)	38.375 ± 20.097 (n=324)	57.621 ± 48.381 (n=158)	<0.001	Fracture ↑	37.524 ± 19.138 (n=259)	59.830 ± 56.264 (n=106)	<0.001	Fracture ↑	41.766 ± 23.392 (n=65)	53.117 ± 25.637 (n=52)	0.003	Fracture ↑
		Blood pro-inflammatory	IL-6 (Plasma)	159.290 ± 158.528 (n=324)	209.209 ± 194.147 (n=158)	0.003	Fracture ↑	155.054 ± 163.091 (n=259)	175.485 ± 165.901 (n=106)	0.175	Fracture ↑	176.169 ± 138.731 (n=65)	277.953 ± 228.448 (n=52)	0.013	Fracture ↑
		Blood pro-inflammatory	IL-8 (Plasma)	18.343 ± 61.197 (n=324)	14.961 ± 46.868 (n=158)	0.081	Cardiac ↓	17.994 ± 67.044 (n=259)	16.366 ± 56.914 (n=106)	0.098	Cardiac ↓	19.734 ± 27.893 (n=65)	12.097 ± 8.975 (n=52)	0.110	Cardiac ↓
		Blood pro-inflammatory	TNFα (Plasma)	2.901 ± 3.318 (n=324)	5.350 ± 11.981 (n=158)	<0.001	Fracture ↑	2.701 ± 3.399 (n=259)	5.602 ± 14.418 (n=106)	<0.001	Fracture ↑	3.697 ± 2.860 (n=65)	4.835 ± 3.676 (n=52)	0.011	Fracture ↑
		Blood pro-inflammatory	MCP-1 (Plasma)	244.067 ± 157.937 (n=324)	231.135 ± 130.858 (n=158)	0.790	Cardiac ↓	232.427 ± 157.298 (n=259)	212.962 ± 109.229 (n=106)	0.576	Cardiac ↓	290.448 ± 153.010 (n=65)	268.180 ± 161.446 (n=52)	0.352	Cardiac ↓
		Blood pro-inflammatory	MIP-1α (Plasma)	5.933 ± 4.421 (n=321)	6.605 ± 3.787 (n=158)	0.001	Fracture ↑	5.320 ± 3.276 (n=256)	6.036 ± 3.523 (n=106)	0.007	Fracture ↑	8.346 ± 6.895 (n=65)	7.765 ± 4.068 (n=52)	0.677	Cardiac ↓
Blood pro-inflammatory		NGAL (Plasma)	1106.105 ± 524.315 (n=325)	936.200 ± 442.423 (n=158)	0.001	Cardiac ↓	1023.422 ± 488.285 (n=260)	786.655 ± 389.232 (n=106)	<0.001	Cardiac ↓	1436.834 ± 536.640 (n=65)	1241.043 ± 386.548 (n=52)	0.029	Cardiac ↓	
Blood pro-inflammatory		IL-12p40 (Serum)	353.553 ± 226.977 (n=319)	404.642 ± 242.732 (n=148)	0.014	Fracture ↑	320.403 ± 209.396 (n=254)	379.728 ± 241.892 (n=102)	0.021	Fracture ↑	483.092 ± 247.479 (n=65)	459.888 ± 237.941 (n=46)	0.726	Cardiac ↓	
Blood pro-inflammatory		IP10 (Serum)	165.888 ± 189.710 (n=319)	155.056 ± 153.910 (n=148)	0.304	Cardiac ↓	160.697 ± 189.218 (n=254)	154.507 ± 156.851 (n=102)	0.278	Cardiac ↓	186.171 ± 191.740 (n=65)	156.275 ± 148.866 (n=46)	0.776	Cardiac ↓	
Blood pro-inflammatory		sIL2Rα (Serum)	0.217 ± 0.199 (n=319)	0.272 ± 0.325 (n=147)	0.001	Fracture ↑	0.208 ± 0.211 (n=254)	0.260 ± 0.359 (n=101)	0.005	Fracture ↑	0.252 ± 0.143 (n=65)	0.300 ± 0.233 (n=46)	0.325	Fracture ↑	

Supplementary File 2: Biomarker ratios comparisons between cardiac and orthopaedic surgery patients pre- and post-operative.

Ratio type	Ratio	All Patients				Non-AKI Patients				AKI Patients				
		Cardiac Ratio	Orthopaedic Ratio	p-value	Change	Cardiac Ratio	Orthopaedic Ratio	p-value	Change	Cardiac Ratio	Orthopaedic Ratio	p-value	Change	
Pre-operative	sTNFR1 (Urine)/NGAL (Plasma)	0.002 ± 0.008 (n=313)	0.004 ± 0.008 (n=163)	<0.001	Orthopaedic ↑	0.002 ± 0.009 (n=249)	0.004 ± 0.003 (n=112)	<0.001	Orthopaedic ↑	0.001 ± 0.001 (n=64)	0.003 ± 0.003 (n=31)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/IL-12p40 (Serum)	0.003 ± 0.008 (n=319)	0.011 ± 0.017 (n=157)	<0.001	Orthopaedic ↑	0.003 ± 0.008 (n=255)	0.012 ± 0.019 (n=109)	<0.001	Orthopaedic ↑	0.003 ± 0.011 (n=64)	0.009 ± 0.011 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/MCP-1 (Plasma)	0.231 ± 0.24 (n=309)	0.629 ± 0.623 (n=163)	<0.001	Orthopaedic ↑	0.227 ± 0.228 (n=245)	0.63 ± 0.603 (n=112)	<0.001	Orthopaedic ↑	0.244 ± 0.296 (n=64)	0.627 ± 0.532 (n=51)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/TNFα (Plasma)	0.359 ± 0.361 (n=312)	1.02 ± 0.905 (n=163)	<0.001	Orthopaedic ↑	0.36 ± 0.371 (n=248)	1.03 ± 0.975 (n=112)	<0.001	Orthopaedic ↑	0.359 ± 0.327 (n=64)	0.988 ± 0.736 (n=51)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/MCP-1 (Plasma)	0.007 ± 0.009 (n=312)	0.018 ± 0.016 (n=163)	<0.001	Orthopaedic ↑	0.007 ± 0.009 (n=248)	0.017 ± 0.015 (n=112)	<0.001	Orthopaedic ↑	0.006 ± 0.006 (n=64)	0.019 ± 0.018 (n=51)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/IL-6 (Plasma)	0.331 ± 0.381 (n=312)	0.886 ± 0.109 (n=163)	<0.001	Cardiac ↓	0.344 ± 0.399 (n=248)	0.887 ± 0.111 (n=112)	<0.001	Cardiac ↓	0.28 ± 0.299 (n=64)	0.883 ± 0.108 (n=51)	<0.001	Cardiac ↓	
	sTNFR1 (Urine)/IP-10 (Serum)	0.907 ± 0.039 (n=319)	0.021 ± 0.035 (n=157)	<0.001	Orthopaedic ↑	0.907 ± 0.031 (n=255)	0.023 ± 0.039 (n=109)	<0.001	Orthopaedic ↑	0.907 ± 0.037 (n=64)	0.03 ± 0.026 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/IL-8 (Plasma)	0.272 ± 0.299 (n=312)	0.519 ± 0.522 (n=163)	<0.001	Orthopaedic ↑	0.272 ± 0.287 (n=248)	0.517 ± 0.519 (n=112)	<0.001	Orthopaedic ↑	0.275 ± 0.344 (n=64)	0.525 ± 0.533 (n=51)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/sIL2Rα (Serum)	6.39 ± 10.4 (n=319)	18.8 ± 22 (n=157)	<0.001	Orthopaedic ↑	6.26 ± 9.68 (n=255)	18.3 ± 23 (n=109)	<0.001	Orthopaedic ↑	6.9 ± 12.6 (n=64)	19.9 ± 19.7 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/NGAL (Plasma)	0.003 ± 0.01 (n=313)	0.005 ± 0.004 (n=162)	<0.001	Orthopaedic ↑	0.003 ± 0.012 (n=249)	0.006 ± 0.004 (n=112)	<0.001	Orthopaedic ↑	0.005 ± 0.004 (n=64)	0.005 ± 0.004 (n=50)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/IL-12p40 (Serum)	0.004 ± 0.008 (n=319)	0.016 ± 0.026 (n=156)	<0.001	Orthopaedic ↑	0.004 ± 0.008 (n=255)	0.018 ± 0.029 (n=109)	<0.001	Orthopaedic ↑	0.004 ± 0.007 (n=64)	0.019 ± 0.015 (n=47)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/MCP-1 (Plasma)	0.389 ± 0.449 (n=309)	0.895 ± 0.719 (n=162)	<0.001	Orthopaedic ↑	0.389 ± 0.407 (n=245)	0.902 ± 0.719 (n=112)	<0.001	Orthopaedic ↑	0.458 ± 0.581 (n=64)	0.881 ± 0.734 (n=50)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/TNFα (Plasma)	0.585 ± 0.648 (n=312)	1.47 ± 1.16 (n=162)	<0.001	Orthopaedic ↑	0.57 ± 0.644 (n=248)	1.5 ± 1.26 (n=112)	<0.001	Orthopaedic ↑	0.643 ± 0.684 (n=64)	1.38 ± 0.95 (n=50)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/MCP-1 (Plasma)	0.011 ± 0.014 (n=312)	0.026 ± 0.022 (n=162)	<0.001	Orthopaedic ↑	0.011 ± 0.015 (n=248)	0.026 ± 0.021 (n=112)	<0.001	Orthopaedic ↑	0.011 ± 0.013 (n=64)	0.027 ± 0.023 (n=50)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/IL-6 (Plasma)	0.544 ± 0.693 (n=312)	0.132 ± 0.174 (n=162)	<0.001	Cardiac ↓	0.546 ± 0.691 (n=248)	0.138 ± 0.189 (n=112)	<0.001	Cardiac ↓	0.511 ± 0.703 (n=64)	0.118 ± 0.134 (n=50)	<0.001	Cardiac ↓	
	sTNFR2 (Urine)/IP-10 (Serum)	0.011 ± 0.014 (n=319)	0.044 ± 0.051 (n=156)	<0.001	Orthopaedic ↑	0.011 ± 0.015 (n=255)	0.046 ± 0.057 (n=109)	<0.001	Orthopaedic ↑	0.012 ± 0.011 (n=64)	0.04 ± 0.033 (n=47)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/IL-8 (Plasma)	0.455 ± 0.564 (n=312)	0.75 ± 0.66 (n=162)	<0.001	Orthopaedic ↑	0.437 ± 0.518 (n=248)	0.771 ± 0.677 (n=112)	<0.001	Orthopaedic ↑	0.522 ± 0.716 (n=64)	0.705 ± 0.627 (n=50)	0.002	Orthopaedic ↑	
	sTNFR2 (Urine)/sIL2Rα (Serum)	10.5 ± 16.9 (n=319)	27.4 ± 31.5 (n=156)	<0.001	Orthopaedic ↑	9.93 ± 14.6 (n=255)	27.4 ± 34.2 (n=109)	<0.001	Orthopaedic ↑	12.5 ± 24 (n=64)	27.4 ± 24.5 (n=47)	<0.001	Orthopaedic ↑	
	IL-1Ra (Urine)/NGAL (Plasma)	5.27 ± 13.3 (n=301)	5.48 ± 7.93 (n=152)	0.206	Orthopaedic ↑	5.27 ± 14.3 (n=238)	6.47 ± 8.95 (n=103)	0.023	Orthopaedic ↑	5.27 ± 8.85 (n=63)	3.4 ± 4.56 (n=49)	0.511	Cardiac ↓	
	IL-1Ra (Urine)/IL-12p40 (Serum)	18.9 ± 202 (n=307)	21.5 ± 63.6 (n=147)	<0.001	Orthopaedic ↑	21.8 ± 227 (n=244)	27.3 ± 75.6 (n=101)	<0.001	Orthopaedic ↑	7.7 ± 14.4 (n=63)	8.58 ± 12.8 (n=46)	0.103	Orthopaedic ↑	
IL-1Ra (Urine)/MCP-1 (Plasma)	729 ± 1260 (n=297)	922 ± 1390 (n=152)	0.377	Orthopaedic ↑	710 ± 1260 (n=234)	1050 ± 1520 (n=103)	0.109	Orthopaedic ↑	800 ± 1260 (n=63)	652 ± 1010 (n=49)	0.565	Cardiac ↓		
IL-1Ra (Urine)/TNFα (Plasma)	1320 ± 2750 (n=301)	1800 ± 2700 (n=152)	0.453	Orthopaedic ↑	1220 ± 2420 (n=238)	1890 ± 3130 (n=103)	0.180	Orthopaedic ↑	1680 ± 3760 (n=63)	978 ± 1230 (n=49)	0.751	Cardiac ↓		
IL-1Ra (Urine)/MCP-1 (Plasma)	22.4 ± 32 (n=301)	25.4 ± 35 (n=152)	0.186	Orthopaedic ↑	21.9 ± 35 (n=238)	28.4 ± 39.7 (n=103)	0.044	Orthopaedic ↑	24.7 ± 45.6 (n=63)	17.2 ± 25.7 (n=49)	0.664	Cardiac ↓		
IL-1Ra (Urine)/IL-6 (Plasma)	1250 ± 2770 (n=301)	138 ± 286 (n=152)	<0.001	Cardiac ↓	1280 ± 2510 (n=238)	162 ± 332 (n=103)	<0.001	Cardiac ↓	1200 ± 3600 (n=63)	3.4 ± 4.56 (n=49)	<0.001	Cardiac ↓		
IL-1Ra (Urine)/IP-10 (Serum)	28.4 ± 76.5 (n=307)	50.7 ± 128 (n=147)	<0.001	Orthopaedic ↑	28.9 ± 82.1 (n=244)	61.5 ± 152 (n=101)	<0.001	Orthopaedic ↑	26.3 ± 49.8 (n=63)	26.9 ± 36.3 (n=46)	0.172	Orthopaedic ↑		
IL-1Ra (Urine)/IL-8 (Plasma)	924 ± 1780 (n=301)	774 ± 1270 (n=152)	0.022	Cardiac ↓	851 ± 1430 (n=238)	926 ± 1490 (n=103)	0.194	Orthopaedic ↑	1200 ± 2710 (n=63)	456 ± 481 (n=49)	0.058	Cardiac ↓		
IL-1Ra (Urine)/sIL2Rα (Serum)	19400 ± 38500 (n=307)	26300 ± 40200 (n=147)	0.071	Orthopaedic ↑	17800 ± 34100 (n=244)	29500 ± 43600 (n=101)	0.022	Orthopaedic ↑	25500 ± 52100 (n=63)	19030 ± 30600 (n=46)	0.871	Cardiac ↓		
Urine anti-inflammatory / Blood anti-inflammatory (R2)	sTNFR1 (Urine)/sTNFR1 (Serum)	2.1 ± 2.35 (n=319)	4.05 ± 3.02 (n=157)	<0.001	Orthopaedic ↑	2.23 ± 2.52 (n=255)	4.14 ± 2.98 (n=109)	<0.001	Orthopaedic ↑	1.6 ± 1.38 (n=64)	3.85 ± 3.13 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/sTNFR2 (Serum)	2.4 ± 3.32 (n=319)	5.84 ± 10.2 (n=157)	<0.001	Orthopaedic ↑	2.62 ± 3.65 (n=255)	6.29 ± 11.6 (n=109)	<0.001	Orthopaedic ↑	1.51 ± 1.31 (n=64)	4.82 ± 6.65 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/sTNFR1 (Serum)	3.44 ± 3.81 (n=319)	5.96 ± 4.3 (n=156)	<0.001	Orthopaedic ↑	3.56 ± 4.01 (n=255)	6.26 ± 4.44 (n=109)	<0.001	Orthopaedic ↑	2.96 ± 2.84 (n=64)	5.28 ± 3.89 (n=47)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/sTNFR2 (Serum)	3.92 ± 6.38 (n=319)	8.65 ± 14.1 (n=156)	<0.001	Orthopaedic ↑	4.21 ± 6.88 (n=255)	9.51 ± 16 (n=109)	<0.001	Orthopaedic ↑	2.76 ± 2.68 (n=64)	6.64 ± 8.33 (n=47)	<0.001	Orthopaedic ↑	
	sTNFR1 (Urine)/sTNFR1 (Serum)	7090 ± 12500 (n=307)	8160 ± 9280 (n=147)	0.122	Cardiac ↓	7070 ± 12500 (n=244)	7320 ± 10600 (n=101)	0.701	Orthopaedic ↑	7170 ± 12700 (n=63)	3680 ± 4710 (n=46)	0.130	Cardiac ↓	
	IL-1Ra (Urine)/sTNFR2 (Serum)	8930 ± 15900 (n=307)	7100 ± 10700 (n=147)	0.411	Cardiac ↓	8940 ± 15200 (n=244)	8410 ± 12000 (n=101)	0.784	Orthopaedic ↑	7880 ± 16800 (n=63)	4230 ± 6380 (n=46)	0.298	Cardiac ↓	
	sTNFR2 (Urine)/H-FABP (Serum)	0.154 ± 0.176 (n=316)	0.296 ± 0.274 (n=158)	<0.001	Orthopaedic ↑	0.158 ± 0.182 (n=253)	0.317 ± 0.29 (n=111)	<0.001	Orthopaedic ↑	0.14 ± 0.162 (n=63)	0.254 ± 0.228 (n=48)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/VEGF (Plasma)	0.027 ± 0.038 (n=312)	0.076 ± 0.088 (n=163)	<0.001	Orthopaedic ↑	0.028 ± 0.039 (n=248)	0.073 ± 0.087 (n=112)	<0.001	Orthopaedic ↑	0.028 ± 0.026 (n=64)	0.084 ± 0.09 (n=51)	<0.001	Orthopaedic ↑	
	sTNFR2 (Urine)/H-FABP (Serum)	0.248 ± 0.286 (n=316)	0.437 ± 0.372 (n=162)	<0.001	Orthopaedic ↑	0.245 ± 0.278 (n=253)	0.474 ± 0.395 (n=111)	<0.001	Orthopaedic ↑	0.261 ± 0.318 (n=63)	0.349 ± 0.296 (n=47)	0.007	Orthopaedic ↑	
	sTNFR2 (Urine)/VEGF (Plasma)	0.045 ± 0.063 (n=312)	0.108 ± 0.103 (n=163)	<0.001	Orthopaedic ↑	0.045 ± 0.065 (n=248)	0.105 ± 0.102 (n=112)	<0.001	Orthopaedic ↑	0.047 ± 0.052 (n=64)	0.114 ± 0.106 (n=50)	<0.001	Orthopaedic ↑	
	IL-1Ra (Urine)/H-FABP (Serum)	536 ± 1060 (n=304)	498 ± 855 (n=151)	0.103	Cardiac ↓	545 ± 1080 (n=242)	623 ± 991 (n=103)	0.956	Orthopaedic ↑	504 ± 1000 (n=62)	230 ± 308 (n=48)	0.103	Cardiac ↓	
	IL-1Ra (Urine)/VEGF (Plasma)	89 ± 156 (n=301)	102 ± 160 (n=152)	0.432	Orthopaedic ↑	89.8 ± 152 (n=238)	115 ± 181 (n=103)	0.375	Orthopaedic ↑	101 ± 172 (n=63)	75.2 ± 102 (n=49)	1.005	Cardiac ↓	
	sTNFR1 (Urine)/Midkine (Serum)	0.001 ± 0.002 (n=263)	0.003 ± 0.004 (n=114)	<0.001	Orthopaedic ↑	0.002 ± 0.002 (n=205)	0.004 ± 0.005 (n=78)	<0.001	Orthopaedic ↑	0.001 ± 0.001 (n=58)	0.003 ± 0.003 (n=36)	0.014	Orthopaedic ↑	
	sTNFR2 (Urine)/Midkine (Serum)	0.002 ± 0.003 (n=263)	0.004 ± 0.006 (n=114)	<0.001	Orthopaedic ↑	0.002 ± 0.003 (n=205)	0.005 ± 0.006 (n=78)	<0.001	Orthopaedic ↑	0.002 ± 0.002 (n=58)	0.003 ± 0.004 (n=36)	0.095	Orthopaedic ↑	
	IL-1Ra (Urine)/Midkine (Serum)	5.39 ± 11.9 (n=263)	4.23 ± 8.89 (n=112)	0.035	Cardiac ↓	5.72 ± 10.5 (n=205)	5.32 ± 10.6 (n=75)	0.468	Cardiac ↓	4.31 ± 6.67 (n=58)	2.003 ± 2.65 (n=37)	0.016	Cardiac ↓	
	Urine anti-inflammatory / Blood proinflammatory (R1)	sTNFR1 (Urine)/NGAL (Plasma)	0.008 ± 0.006 (n=315)	0.007 ± 0.005 (n=147)	0.036	Cardiac ↓	0.008 ± 0.005 (n=250)	0.007 ± 0.005 (n=97)	0.100	Cardiac ↓	0.007 ± 0.006 (n=65)	0.006 ± 0.003 (n=50)	0.507	Cardiac ↓
		sTNFR2 (Urine)/IL-12p40 (Serum)	0.028 ± 0.023 (n=312)	0.021 ± 0.025 (n=138)	<0.001	Cardiac ↓	0.023 ± 0.024 (n=247)	0.019 ± 0.023 (n=93)	<0.001	Cardiac ↓	0.023 ± 0.024 (n=65)	0.024 ± 0.029 (n=45)	0.325	Orthopaedic ↑
		sTNFR1 (Urine)/MCP-1 (Plasma)	1.58 ± 1.27 (n=311)	1.04 ± 0.89 (n=147)	<0.001	Cardiac ↓	1.63 ± 1.32 (n=246)	1 ± 0.812 (n=97)	<0.001	Cardiac ↓	1.39 ± 1.02 (n=65)	1.12 ± 1.03 (n=50)	0.021	Cardiac ↓
		sTNFR1 (Urine)/TNFα (Plasma)	2.2 ± 2.05 (n=315)	3.58 ± 1.14 (n=147)	<0.001	Cardiac ↓	2.1 ± 2.04 (n=246)	3.58 ± 1.14 (n=97)	<0.001	Cardiac ↓	2.2 ± 2.04 (n=65)	3.7 ± 1.24 (n=45)	<0.001	Cardiac ↓
		sTNFR1 (Urine)/MCP-1 (Plasma)	0.036 ± 0.025 (n=315)	0.028 ± 0.022 (n=147)	<0.001	Cardiac ↓	0.037 ± 0.026 (n=250)	0.027 ± 0.021 (n=97)	<0.001	Cardiac ↓	0.034 ± 0.022 (n=65)	0.031 ± 0.022 (n=50)	0.258	Cardiac ↓
sTNFR1 (Urine)/IL-6 (Plasma)		0.087 ± 0.234 (n=315)	0.057 ± 0.101 (n=147)	<0.001	Cardiac ↓	0.088 ± 0.257 (n=250)	0.065 ± 0.12 (n=97)	<0.001	Cardiac ↓	0.084 ± 0.104 (n=65)	0.042 ± 0.039 (n=50)	0.001	Cardiac ↓	
sTNFR1 (Urine)/IP-10 (Serum)		0.1 ± 0.209 (n=312)	0.054 ± 0.055 (n=138)	<0.001	Cardiac ↓	0.107 ± 0.232 (n=247)	0.051 ± 0.058 (n=93)	<0.001	Cardiac ↓	0.076 ± 0.109 (n=65)	0.06 ± 0.049 (n=45)	0.185	Cardiac ↓	
sTNFR1 (Urine)/IL-8 (Plasma)		0.833 ± 0.858 (n=315)	0.732 ± 0.67 (n=147)	0.026	Cardiac ↓	0.838 ± 0.852 (n=250)	0.895 ± 0.65 (n=97)	0.011	Cardiac ↓	0.81 ± 0.886 (n=65)	0.808 ± 0.708 (n=50)	0.998	Cardiac ↓	
sTNFR2 (Urine)/NGAL (Plasma)		0.009 ± 0.006 (n=316)	0.008 ± 0.005 (n=147)	0.025	Cardiac ↓	0.01 ± 0.006 (n=251)	0.009 ± 0.006 (n=97)	0.205	Cardiac ↓	0.009 ± 0.005 (n=65)	0.006 ± 0.003 (n=50)	0.253	Cardiac ↓	
sTNFR2 (Urine)/IL-12p40 (Serum)		0.032 ± 0.023 (n=313)	0.023 ± 0.025 (n=138)	<0.001	Cardiac ↓	0.034 ± 0.024 (n=248)	0.023 ± 0.026 (n=93)	<0.001	Cardiac ↓	0.024 ± 0.017 (n=65)	0.023 ± 0.022 (n=45)	0.217	Cardiac ↓	
sTNFR2 (Urine)/MCP-1 (Plasma)		1.88 ± 1.55 (n=312)	1.21 ± 1.01 (n=147)	<0.001	Cardiac ↓	1.96 ± 1.84 (n=247)	1.23 ± 1.02 (n=97)	<0.001	Cardiac ↓	1.64 ± 1.51 (n=65)	1.15 ± 1.02 (n=50)			

Supplementary File 3: Delta (Δ) differences in biomarkers measured pre- and post-operatively between cardiac and orthopaedic surgery patients.

Marker Type	Biomarker	All Patients				Non-AKI Patients				AKI Patients			
		Cardiac Δ Difference [mean \pm SD]	Fracture Δ Difference [mean \pm SD]	p value	Change	Cardiac Δ Difference [mean \pm SD]	Fracture Δ Difference [mean \pm SD]	p value	Change	Cardiac Δ Difference [mean \pm SD]	Fracture Δ Difference [mean \pm SD]	p value	Change
Blood anti-inflammatory	sTNFR1 (Serum)	0.516 \pm 1.776 (n=316)	0.273 \pm 0.352 (n=142)	<0.001	Cardiac \uparrow	0.516 \pm 1.973 (n=253)	0.215 \pm 0.339 (n=96)	<0.001	Cardiac \uparrow	0.512 \pm 0.437 (n=63)	0.392 \pm 0.352 (n=46)	0.014	Cardiac \uparrow
Blood anti-inflammatory	sTNFR2 (Serum)	0.421 \pm 0.470 (n=316)	0.348 \pm 0.578 (n=142)	0.115	Cardiac \uparrow	0.383 \pm 0.376 (n=253)	0.247 \pm 0.612 (n=96)	0.002	Cardiac \uparrow	0.574 \pm 0.720 (n=63)	0.560 \pm 0.433 (n=46)	0.665	Cardiac \uparrow
Blood anti-inflammatory	IL-1Ra (Serum)	542.734 \pm 537.269 (n=316)	259.122 \pm 545.411 (n=143)	<0.001	Cardiac \uparrow	477.137 \pm 476.183 (n=253)	156.814 \pm 487.020 (n=97)	<0.001	Cardiac \uparrow	806.165 \pm 675.920 (n=63)	474.860 \pm 602.123 (n=46)	0.002	Cardiac \uparrow
Blood anti-inflammatory	IL-10 (Plasma)	4.162 \pm 9.650 (n=314)	1.951 \pm 14.523 (n=152)	<0.001	Cardiac \uparrow	4.154 \pm 10.392 (n=251)	1.019 \pm 8.788 (n=101)	<0.001	Cardiac \uparrow	4.192 \pm 5.886 (n=63)	3.795 \pm 21.848 (n=51)	<0.001	Cardiac \uparrow
Blood hypoperfusion	H-FABP (Serum)	29.770 \pm 65.502 (n=314)	18.577 \pm 26.113 (n=149)	0.090	Cardiac \uparrow	22.932 \pm 61.590 (n=252)	12.080 \pm 16.722 (n=101)	0.004	Cardiac \uparrow	57.564 \pm 73.674 (n=62)	32.248 \pm 35.647 (n=48)	0.236	Cardiac \uparrow
Blood hypoperfusion	VEGF (Plasma)	3.077 \pm 25.534 (n=314)	1.082 \pm 52.302 (n=152)	0.394	Cardiac \uparrow	4.370 \pm 23.330 (n=251)	2.020 \pm 60.507 (n=101)	0.446	Cardiac \uparrow	-2.075 \pm 32.606 (n=63)	-0.776 \pm 30.555 (n=51)	0.423	Orthopaedic \uparrow
Blood pro-inflammatory	IL-6 (Plasma)	152.283 \pm 165.816 (n=314)	137.746 \pm 211.842 (n=152)	0.026	Cardiac \uparrow	147.584 \pm 171.605 (n=251)	97.552 \pm 198.525 (n=101)	<0.001	Cardiac \uparrow	171.007 \pm 140.057 (n=63)	217.347 \pm 216.743 (n=51)	0.596	Orthopaedic \uparrow
Blood pro-inflammatory	IL-8 (Plasma)	14.256 \pm 61.985 (n=314)	4.846 \pm 48.934 (n=152)	<0.001	Cardiac \uparrow	14.072 \pm 68.308 (n=251)	5.335 \pm 59.760 (n=101)	<0.001	Cardiac \uparrow	14.990 \pm 24.121 (n=63)	3.876 \pm 9.359 (n=51)	<0.001	Cardiac \uparrow
Blood pro-inflammatory	TNF α (Plasma)	0.219 \pm 7.112 (n=314)	1.181 \pm 10.803 (n=152)	0.279	Orthopaedic \uparrow	0.025 \pm 7.854 (n=251)	1.469 \pm 13.186 (n=101)	0.375	Orthopaedic \uparrow	0.988 \pm 2.430 (n=63)	0.612 \pm 2.051 (n=51)	0.376	Cardiac \uparrow
Blood pro-inflammatory	MCP-1 (Plasma)	108.568 \pm 155.348 (n=314)	28.947 \pm 111.519 (n=152)	<0.001	Cardiac \uparrow	100.204 \pm 156.135 (n=251)	26.376 \pm 121.886 (n=101)	<0.001	Cardiac \uparrow	141.891 \pm 148.733 (n=63)	34.039 \pm 88.353 (n=51)	<0.001	Cardiac \uparrow
Blood pro-inflammatory	MIP-1 α (Plasma)	-0.347 \pm 29.347 (n=310)	0.579 \pm 3.088 (n=152)	<0.001	Orthopaedic \uparrow	0.451 \pm 17.604 (n=247)	0.528 \pm 3.048 (n=101)	0.001	Orthopaedic \uparrow	-3.477 \pm 55.229 (n=63)	0.679 \pm 3.194 (n=51)	0.001	Orthopaedic \uparrow
Blood pro-inflammatory	NGAL (Plasma)	452.044 \pm 420.025 (n=315)	44.540 \pm 380.879 (n=152)	<0.001	Cardiac \uparrow	398.994 \pm 383.209 (n=252)	12.968 \pm 389.872 (n=101)	<0.001	Cardiac \uparrow	664.244 \pm 491.721 (n=63)	107.064 \pm 357.921 (n=51)	<0.001	Cardiac \uparrow
Blood pro-inflammatory	IL-12p40 (Serum)	-120.941 \pm 185.884 (n=316)	-35.119 \pm 153.503 (n=143)	<0.001	Orthopaedic \uparrow	-122.772 \pm 171.729 (n=253)	-24.240 \pm 145.572 (n=97)	<0.001	Orthopaedic \uparrow	-113.589 \pm 235.832 (n=63)	-58.058 \pm 168.387 (n=46)	0.007	Orthopaedic \uparrow
Blood pro-inflammatory	IP10 (Serum)	25.524 \pm 176.165 (n=316)	13.617 \pm 131.499 (n=143)	0.181	Cardiac \uparrow	24.741 \pm 175.369 (n=253)	15.071 \pm 117.958 (n=97)	0.108	Cardiac \uparrow	28.670 \pm 180.720 (n=63)	10.550 \pm 157.696 (n=46)	0.988	Cardiac \uparrow
Blood pro-inflammatory	sIL2Ra (Serum)	0.021 \pm 0.166 (n=316)	0.033 \pm 0.126 (n=142)	0.143	Orthopaedic \uparrow	0.012 \pm 0.174 (n=253)	0.021 \pm 0.127 (n=96)	0.246	Orthopaedic \uparrow	0.058 \pm 0.123 (n=63)	0.058 \pm 0.122 (n=46)	0.980	Orthopaedic \uparrow
Blood pro-inflammatory	IL-2 (Plasma)	-0.157 \pm 3.820 (n=314)	0.021 \pm 2.877 (n=152)	0.847	Orthopaedic \uparrow	0.004 \pm 4.048 (n=251)	-0.028 \pm 3.506 (n=101)	0.176	Cardiac \uparrow	-0.802 \pm 2.654 (n=63)	0.117 \pm 0.628 (n=51)	0.011	Orthopaedic \uparrow
Blood pro-inflammatory	IL-4 (Plasma)	-0.106 \pm 2.607 (n=314)	0.032 \pm 0.998 (n=152)	0.583	Orthopaedic \uparrow	-0.136 \pm 2.895 (n=251)	0.025 \pm 1.036 (n=101)	0.262	Orthopaedic \uparrow	0.010 \pm 0.699 (n=63)	0.047 \pm 0.930 (n=51)	0.637	Orthopaedic \uparrow
Blood pro-inflammatory	IL-1 α (Plasma)	0.239 \pm 3.640 (n=314)	0.029 \pm 0.521 (n=152)	0.998	Cardiac \uparrow	0.327 \pm 4.061 (n=251)	0.040 \pm 0.612 (n=101)	0.905	Cardiac \uparrow	-0.111 \pm 0.498 (n=63)	0.005 \pm 0.265 (n=51)	0.515	Orthopaedic \uparrow
Blood pro-inflammatory	IL-1 β (Plasma)	1.547 \pm 29.416 (n=314)	0.019 \pm 1.240 (n=152)	0.916	Cardiac \uparrow	2.011 \pm 32.885 (n=251)	0.009 \pm 1.425 (n=101)	0.837	Cardiac \uparrow	-0.298 \pm 1.878 (n=63)	0.038 \pm 0.764 (n=51)	0.735	Orthopaedic \uparrow
Blood pro-inflammatory	IFN γ (Plasma)	-0.184 \pm 2.061 (n=314)	-0.150 \pm 2.340 (n=152)	0.859	Orthopaedic \uparrow	-0.105 \pm 1.669 (n=251)	-0.261 \pm 2.646 (n=101)	0.997	Cardiac \uparrow	-0.500 \pm 3.177 (n=63)	0.070 \pm 1.566 (n=51)	0.681	Orthopaedic \uparrow
Blood pro-inflammatory	GM-CSF (Plasma)	-0.774 \pm 13.265 (n=310)	0.031 \pm 1.107 (n=152)	0.844	Orthopaedic \uparrow	-0.005 \pm 0.440 (n=247)	-0.057 \pm 0.549 (n=101)	0.812	Cardiac \uparrow	-3.788 \pm 29.404 (n=63)	0.206 \pm 1.747 (n=51)	0.945	Orthopaedic \uparrow
Blood pro-inflammatory	sIL6R (Serum)	0.121 \pm 0.668 (n=316)	0.041 \pm 0.650 (n=142)	0.005	Cardiac \uparrow	0.133 \pm 0.584 (n=253)	-0.043 \pm 0.599 (n=96)	0.001	Cardiac \uparrow	0.076 \pm 0.939 (n=63)	0.217 \pm 0.719 (n=46)	0.883	Orthopaedic \uparrow
Blood pro-inflammatory	MMP9 (Serum)	11.518 \pm 33.046 (n=316)	13.637 \pm 71.064 (n=142)	0.367	Orthopaedic \uparrow	10.466 \pm 32.365 (n=253)	9.554 \pm 75.449 (n=96)	0.480	Cardiac \uparrow	15.742 \pm 35.610 (n=63)	22.158 \pm 60.798 (n=46)	0.740	Orthopaedic \uparrow
Blood IRI	Midkine (Serum)	705.269 \pm 1665.164 (n=269)	-130.205 \pm 1923.366 (n=128)	<0.001	Cardiac \uparrow	487.056 \pm 1430.710 (n=211)	-203.931 \pm 1765.125 (n=86)	<0.001	Cardiac \uparrow	1499.114 \pm 2162.882 (n=58)	20.759 \pm 2228.197 (n=42)	0.001	Cardiac \uparrow
Urine IRI	Midkine (Urine)	2254.982 \pm 1619.421 (n=279)	893.048 \pm 2067.282 (n=141)	<0.001	Cardiac \uparrow	2218.478 \pm 1577.520 (n=221)	813.050 \pm 1816.603 (n=93)	<0.001	Cardiac \uparrow	2394.073 \pm 1777.833 (n=58)	1048.045 \pm 2496.632 (n=48)	0.002	Cardiac \uparrow
Urine anti-inflammatory	IL-1Ra (Urine)	10224.628 \pm 11362.783 (n=306)	2889.569 \pm 10199.448 (n=143)	<0.001	Cardiac \uparrow	9628.131 \pm 10717.319 (n=243)	1967.798 \pm 9920.887 (n=96)	<0.001	Cardiac \uparrow	12525.405 \pm 13418.280 (n=63)	4772.336 \pm 10605.196 (n=47)	<0.001	Cardiac \uparrow
Urine anti-inflammatory	sTNFR1 (Urine)	6.361 \pm 3.830 (n=315)	2.466 \pm 3.203 (n=148)	<0.001	Cardiac \uparrow	6.047 \pm 3.522 (n=251)	2.195 \pm 3.174 (n=101)	<0.001	Cardiac \uparrow	7.592 \pm 4.684 (n=64)	3.049 \pm 3.219 (n=47)	<0.001	Cardiac \uparrow
Urine anti-inflammatory	sTNFR2 (Urine)	6.931 \pm 3.744 (n=316)	1.781 \pm 3.455 (n=147)	<0.001	Cardiac \uparrow	6.771 \pm 3.589 (n=252)	1.597 \pm 3.533 (n=101)	<0.001	Cardiac \uparrow	7.561 \pm 4.273 (n=64)	2.185 \pm 3.280 (n=46)	<0.001	Cardiac \uparrow
Urine pro-inflammatory	NGAL (Urine)	139.025 \pm 254.597 (n=306)	159.101 \pm 389.128 (n=143)	0.059	Orthopaedic \uparrow	122.019 \pm 225.255 (n=243)	106.863 \pm 379.538 (n=96)	0.280	Cardiac \uparrow	204.622 \pm 339.584 (n=63)	265.801 \pm 390.651 (n=47)	0.202	Orthopaedic \uparrow
Urine pro-inflammatory	IL-12p40 (Urine)	-1.719 \pm 52.806 (n=317)	2.260 \pm 21.526 (n=148)	0.249	Orthopaedic \uparrow	-0.780 \pm 38.070 (n=253)	2.382 \pm 25.670 (n=101)	0.238	Orthopaedic \uparrow	-5.434 \pm 90.398 (n=64)	1.996 \pm 6.943 (n=47)	0.549	Orthopaedic \uparrow
Urine pro-inflammatory	IP-10 (Urine)	18.522 \pm 102.550 (n=317)	55.500 \pm 223.671 (n=147)	<0.001	Orthopaedic \uparrow	11.523 \pm 88.575 (n=253)	54.839 \pm 260.808 (n=101)	0.011	Orthopaedic \uparrow	46.191 \pm 142.805 (n=64)	56.953 \pm 105.620 (n=46)	0.092	Orthopaedic \uparrow
Urine pro-inflammatory	sIL2Ra (Urine)	-0.006 \pm 0.074 (n=316)	0.051 \pm 0.313 (n=147)	<0.001	Orthopaedic \uparrow	-0.009 \pm 0.073 (n=252)	0.062 \pm 0.376 (n=100)	0.001	Orthopaedic \uparrow	0.006 \pm 0.078 (n=64)	0.027 \pm 0.073 (n=47)	0.189	Orthopaedic \uparrow
Urine pro-inflammatory	sIL6R (Urine)	0.033 \pm 0.218 (n=316)	0.047 \pm 0.173 (n=148)	0.936	Orthopaedic \uparrow	0.036 \pm 0.149 (n=252)	0.052 \pm 0.198 (n=101)	0.576	Orthopaedic \uparrow	0.019 \pm 0.387 (n=64)	0.038 \pm 0.101 (n=47)	0.418	Orthopaedic \uparrow
Urine pro-inflammatory	MMP9 (Urine)	-3.717 \pm 50.996 (n=315)	-8.425 \pm 40.275 (n=147)	<0.001	Cardiac \uparrow	-4.353 \pm 56.789 (n=252)	-11.883 \pm 46.894 (n=101)	<0.001	Cardiac \uparrow	-1.171 \pm 10.309 (n=63)	-0.834 \pm 17.037 (n=46)	0.050	Orthopaedic \uparrow

Delta (Δ) change was calculated as post-operative biomarker value minus pre-operative biomarker for each patient. Statistical significance was determined by Mann-Whitney U test with a Bonferroni corrected p value <0.0015 considered as significant (highlighted bold). Change arrow indicates whether Δ change is higher in cardiac or orthopaedic cohorts. EGF, epidermal growth factor; GM-CSF, granulocyte monocyte-colony stimulating factor; H-FABP, heart-type fatty acid binding protein; IFN γ , interferon gamma; IL-1 α , interleukin-1 alpha; IL-1 β , interleukin-1 beta; IL-1Ra, interleukin-1 receptor antagonist; IL-2, interleukin-2; IL-4, interleukin-4; IL-5, interleukin-5; IL-6, interleukin-6; IL-8, interleukin-8; IL-10, interleukin-10; IL-12p40, interleukin-12 subunit p40; IL-15, interleukin-15; IP-10, interferon gamma-induced protein-10; IRI, ischaemia-reperfusion injury; MCP-1, monocyte chemoattractant protein-1; MIP-1 α , macrophage inflammatory protein-1 α ; n, number of patients; MMP9, matrix metalloproteinase-9; NGAL, neutrophil gelatinase-associated lipocalin; PDGF-BB, platelet-derived growth factor BB; SD, standard deviation; sIL2Ra, soluble interleukin-2 receptor alpha; sIL6R, soluble interleukin-6 receptor; sTNFR1, soluble tumour necrosis factor receptor 1; sTNFR2, soluble tumour necrosis factor receptor 2; TNF α , tumour necrosis factor alpha; VEGF, vascular endothelial growth factor.