

Supplementary material

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Supplementary Table S1. Baseline clinical characteristics, management, and outcomes of patients with history of heart failure admitted for COVID-19 grouped by in-hospital renin-angiotensin-aldosterone system inhibitor use, in-hospital renin-angiotensin-aldosterone system inhibitor withdrawal, and non-renin-angiotensin-aldosterone system inhibitor use.

	In-hospital RAASi use (n=333)	RAASi withdrawal (n=288)	<i>P</i> value*	Non-RAASi use (n=550)	<i>P</i> value**	<i>P</i> value***
Age (years)	76.6 (11.3)	80.8 (10.0)	0.03	82.1 (11.1)	0.01	0.11
Male gender	186 (55.9%)	144 (50.0%)	0.10	291 (52.9%)	0.13	0.20
Comorbidities						
History of smoking	165 (49.5%)	113 (39.2%)	0.02	187 (34.0%)	0.04	0.20
Obesity	136 (40.8%)	89 (30.9%)	0.04	116 (21.1%)	<0.001	0.03
Diabetes mellitus	133 (39.9%)	115 (39.9%)	0.80	166 (30.2%)	0.01	0.02
Hypertension	307 (92.2%)	275 (95.5%)	0.30	527 (70.9%)	<0.001	<0.001
Dyslipidemia	222 (66.7%)	176 (61.1%)	0.19	279 (50.7%)	<0.001	0.03
Chronic kidney disease	71 (21.3%)	64 (22.2%)	0.40	192 (19.6%)	0.39	0.40
Atrial fibrillation	155 (46.5%)	140 (48.6%)	0.34	272 (49.5%)	0.26	0.30
Coronary artery disease	164 (49.2%)	133 (46.2%)	0.19	208 (37.8%)	0.03	0.03
Chronic obstructive pulmonary disease	60 (18.0%)	53 (18.4%)	0.68	91 (16.5%)	0.32	0.21

Stroke	20 (6.0%)	23 (8.0%)	0.19	34 (6.2%)	0.45	0.28
Dementia	42 (12.6%)	52 (18.1%)	0.04	146 (26.5%)	<0.001	0.011
Moderate-severe functional dependence	215 (34.6%)	109 (37.8%)	0.14	280 (50.9%)	<0.001	<0.001
Moderate-severe comorbidity	328 (98.5%)	282 (97.9%)	0.66	541 (98.4%)	0.67	0.60
Preadmission treatment						
RAAS inhibitors	333 (100.0%)	288 (100.0%)	0.99	0	<0.001	<0.001
Statins	209 (62.8%)	156 (54.2%)	0.04	217 (39.5%)	<0.001	0.01
Antiplatelet	91 (27.3%)	93 (32.3%)	0.13	136 (24.7%)	0.11	0.04
Anticoagulant	160 (48.0%)	129 (44.8%)	0.11	261 (47.5%)	0.17	0.20
Metformin	74 (22.2%)	60 (20.8%)	0.31	73 (13.3%)	<0.001	<0.001
DPP-4 inhibitors	65 (19.5%)	57 (19.8%)	0.50	58 (10.5%)	0.01	0.02
SGLT-2 inhibitors	32 (9.6%)	13 (4.5%)	<0.001	7 (1.3%)	<0.001	0.02
GLP-1 receptor agonist	15 (4.5%)	4 (1.4%)	0.04	10 (1.8%)	0.03	0.03
Insulin	76 (22.8%)	43 (14.9%)	0.01	71 (12.9%)	0.008	0.30
Clinical presentation						
Systolic blood pressure, mmHg	131.9 (25.5)	126.8 (27.8)	0.09	128.1 (24.2)	0.32	0.39
Diastolic blood pressure, mmHg	72.0 (14.9)	68.8 (14.0)	0.10	70.2 (14.0)	0.53	0.20
Heart rate, beats/minute	84.2 (17.6)	87.6 (18.7)	0.20	87.9 (20.3)	0.59	0.60
Oxygen saturation, %	92.5 (5.2)	90.2 (8.0)	0.07	92.0 (6.3)	0.46	0.08
Disease severity						
Moderate	230 (69.1%)	190 (66.0%)	0.10	361 (65.6%)	0.09	0.10
Severe	87 (26.1%)	82 (28.5%)		169 (30.8)		
Critical	16 (4.8%)	16 (5.6%)		20 (3.6%)		
Laboratory data						
Blood glucose, mg/dL	130 (118, 142)	154 (121, 165)	0.03	132 (119, 148)	0.23	0.03
Creatinine, md/dL	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)	0.71	1.2 (0.9, 1.8)	0.83	0.90
Blood urea nitrogen, mg/dL	58 (40, 90)	62 (48, 97)	0.03	60 (47, 92)	0.55	0.04
Dehydrogenase lactate, U/L	342 (252, 476)	351 (260, 483)	0.07	354 (261, 484)	0.29	0.40
Aspartate aminotransferase , U/L	34 (23, 50)	52 (33, 60)	0.06	44 (28, 52)	0.15	0.06
Alanine aminotransferase , U/L	28 (18, 36)	32 (20, 39)	0.17	30 (19, 38)	0.33	0.11
Alkaline phosphate, U/L	78 (58, 98)	79 (58, 99)	0.29	88 (61, 103)	0.10	0.10
Bilirubin, mg/dL	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)	0.41	0.6 (0.4, 0.9)	0.29	0.50

Sodium, mmol/L	138 (134, 141)	138 (134, 141)	0.51	139 (134, 142)	0.46	0.39
Potassium, mmol/L	4.2 (3.8, 4.7)	4.2 (3.8, 4.7)	0.60	4.2 (3.8, 4.7)	0.57	0.62
Triglycerides, mg/dL	132 (97, 162)	135 (99, 165)	0.25	120 (89, 155)	0.19	0.12
Kinase creatinine, U/L	175.5 (98.3, 251.1)	214.4 (112.5, 312.5)	0.17	255.1 (138.0, 401.4)	0.08	0.09
Ferritin, mcg/L	744.2 (325.5, 1323.3)	525.3 (231.0, 1056.5)	0.10	878.1 (398.8, 1552.2)	0.18	0.08
Lactate, mmol/L	3.0 (1.8, 4.1)	4.3 (2.1, 5.2)	0.04	2.5 (1.5, 3.5)	0.12	0.04
Troponin I, mcg/L	4.5 (1.1, 5.1)	4.0 (1.0, 4.8)	0.20	6.1 (1.5, 7.5)	0.04	0.04
Interleukin-6, pg/mL	50.5 (20.5, 116.0)	79.0 (25.7, 124.8)	0.04	103.8 (38.9, 139.7)	0.02	0.03
C-Reactive protein, mg/L	85.2 (39.5, 102.3)	90.4 (42.1, 110.3)	0.51	75.2 (35.6, 99.9)	0.20	0.30
Procalcitonin, ng/mL	0.2 (0.1, 0.4)	1.0 (0.3, 1.5)	0.03	0.8 (0.2, 1.2)	0.68	0.09
Albumin, g/dL	3.5 (3.1, 3.9)	3.4 (2.9, 3.8)	0.52	3.4 (2.9, 3.8)	0.76	0.69
Fibrinogen, mg/dL	606.2 (500.0, 687.5)	603.4 (499.8, 684.2)	0.60	591.0 (499.5, 700.0)	0.51	0.41
D-Dimer, ng/ml	1277.5 (689.1, 2289.5)	946.2 (500.0, 1806.3)	0.20	1692.5 (789.8, 2998.0)	0.008	0.005
Hemoglobin, g/dL	12.9 (11.3, 14.2)	12.7 (11.1, 13.9)	0.27	12.5 (11.0, 13.6)	0.26	0.30
Leucocytes, x10 ⁹ /L	6.9 (5.0, 9.7)	6.7 (5.0, 9.5)	0.15	6.8 (5.0, 9.3)	0.92	0.20
Neutrophils, x10 ⁹ /L	5.2 (3.5, 7.7)	5.4 (3.6, 7.9)	0.32	5.7 (3.8, 8.1)	0.11	0.32
Lymphocytes, x10 ⁹ /L	0.9 (0.6, 1.3)	0.8 (0.6, 1.2)	0.50	0.8 (0.6, 1.3)	0.84	0.80
Platelets, x10 ⁹ /L	175 (135, 231)	182 (139, 235)	0.50	185 (140, 237)	0.18	0.15
In-hospital treatment						
Statins	142 (42.6%)	50 (17.4%)	<0.001	90 (16.4%)	<0.001	0.38
Antiplatelet	88 (26.4%)	71 (24.7%)	0.18	99 (18.0%)	<0.001	0.009
Anticoagulant	306 (91.9%)	260 (90.3%)	0.41	494 (89.8%)	0.27	0.38
Hydroxychloroquine	262 (78.7%)	208 (72.2%)	0.11	400 (72.7%)	0.13	0.41
Chloroquine	7 (2.1%)	14 (4.9%)	0.04	11 (2.0%)	0.15	0.51
Lopinavir/ritonavir	150 (45.0%)	114 (39.6%)	0.09	195 (35.5%)	0.003	0.10
Azithromycin	176 (52.9%)	154 (53.5%)	0.33	268 (48.7%)	0.06	0.06
Remdesivir	11 (3.3%)	2 (0.7%)	0.08	1 (0.2%)	0.07	0.21
Interferon- β	40 (12.0%)	31 (10.8%)	0.12	25 (4.5%)	<0.001	0.01
Corticosteroids	137 (41.1%)	120 (41.7%)	0.51	224 (40.7%)	0.50	0.51
Tocilizumab	21 (6.3%)	14 (4.9%)	0.15	18 (3.4%)	0.03	0.09
Outcomes						
In-hospital mortality	117 (35.1%)	137 (47.6%)	0.03	273 (49.6%)	0.02	0.11

ICU admission, mechanical ventilation, or in-hospital mortality	157 (47.1%)	172 (59.7%)	0.03	365 (66.4%)	0.01	0.02
In-hospital complications	218 (65.5%)	216 (75.0%)	0.03	440 (80.0%)	0.02	0.08
Acute heart failure decompensation	103 (30.9%)	110 (38.2%)	0.04	225 (40.9%)	0.03	0.19

Data are shown as mean (standard deviations) or median (first quartile, third quartile) when they did not show a normal distribution, absolute values, and percentages. Values were considered to be statistically significant when $P < 0.05$.

*In-hospital RAASi use versus RAASi withdrawal ** In-hospital RAASi use versus Non-RAASi use *** RAASi withdrawal versus Non-RAASi use

DPP-4: dipeptidyl peptidase-4; GLP-1: glucagon-like peptide-1; ICU: intensive care unit; RAAS: renin-angiotensin-aldosterone system; SGLT-2: sodium-glucose cotransporter 2

Supplementary Table S2. Post-propensity score matching characteristics of patients with history of heart failure admitted for COVID-19 grouped by in-hospital renin-angiotensin-aldosterone system inhibitor use, in-hospital renin-angiotensin-aldosterone system inhibitor withdrawal, and non-renin-angiotensin-aldosterone system inhibitor use.

	In-hospital RAASi use (n=196)	RAASi withdrawal (n=196)	<i>P</i> value	SMD	In-hospital RAASi use (n=236)	Non-RAASi use (n=236)	<i>P</i> value	SMD
Age (years)	78.8 (11.5)	79.1 (11.8)	0.43	0.012	79.5 (11.2)	81.1 (11.1)	0.18	0.023
Male gender	103 (52.6%)	100 (51.0%)	0.40	0.032	127 (53.8%)	125 (53.0%)	0.43	0.016
History of smoking	83 (42.3%)	79 (40.3%)	0.31	0.055	94 (39.8%)	84 (35.6%)	0.15	0.077
Obesity	73 (37.2%)	68 (34.7%)	0.28	0.068	71 (30.1%)	62 (26.3%)	0.21	0.052
Diabetes mellitus	77 (39.3%)	77 (39.3%)	0.82	0.011	79 (33.5%)	71 (30.1%)	0.23	0.051
Hypertension	182 (92.9%)	185 (94.4%)	0.29	0.077	193 (81.8%)	177 (75.0%)	0.18	0.046
Dyslipidemia	125 (63.8%)	120 (61.2%)	0.20	0.081	142 (60.2%)	130 (55.1%)	0.19	0.042
Chronic kidney disease	43 (21.9%)	43 (21.9%)	0.83	0.016	47 (19.9%)	47 (19.9%)	0.87	0.022
Atrial fibrillation	92 (46.9%)	93 (47.4%)	0.61	0.021	111 (47.0%)	116 (49.2%)	0.35	0.040
Coronary artery disease	96 (49.0%)	95 (48.5%)	0.65	0.014	95 (40.3%)	90 (38.1%)	0.23	0.055
Chronic obstructive pulmonary disease	36 (18.4%)	36 (18.4%)	0.87	0.019	40 (16.9%)	39 (16.5%)	0.63	0.039
Stroke	13 (6.6%)	14 (7.1%)	0.31	0.041	14 (5.9%)	14 (5.9%)	0.80	0.019
Dementia	27 (13.8%)	30 (15.3%)	0.24	0.079	34 (14.4%)	45 (19.1%)	0.19	0.072
Moderate-severe functional dependence	69 (35.2%)	72 (36.7%)	0.30	0.044	94 (39.8%)	100 (42.4%)	0.21	0.044
Moderate-severe comorbidity	192 (98.0%)	192 (98.0%)	0.85	0.016	233 (98.7%)	233 (98.7%)	0.83	0.012
Statins	117 (59.7%)	110 (56.1%)	0.20	0.083	118 (50.0%)	101 (42.8%)	0.12	0.086
Antiplatelet	55 (28.1%)	30 (30.6%)	0.23	0.089	61 (25.8%)	58 (24.6%)	0.48	0.050

Anticoagulant	91 (46.4%)	89 (45.4%)	0.52	0.021	113 (47.9%)	113 (47.9%)	0.87	0.019
Disease severity								
Moderate	133 (67.9%)	132 (67.3%)	0.21	0.079	160 (67.8%)	155 (65.7%)	0.28	0.049
Severe	53 (27.0%)	53 (27.0%)			66 (28.0%)	71 (30.1%)		
Critical	10 (5.1%)	11 (5.7%)			10 (4.2%)	10 (4.2%)		
Blood glucose, mg/dL	140 (123, 168)	148 (131, 175)	0.10	0.091	142 (125, 170)	140 (123, 169)	0.52	0.021
Creatinine, md/dL	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)	0.79	0.014	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)	0.86	0.010
Blood urea nitrogen, mg/dL	59 (40, 90)	61 (48, 97)	0.19	0.032	59 (40, 90)	60 (48, 97)	0.61	0.028
Ferritin, mcg/L	744.2 (325.5, 1323.3)	625.0 (310.0, 1215.2)	0.20	0.067	765.4 (335.1, 1325.4)	805.0 (368.4, 1382.5)	0.19	0.039
Lactate, mmol/L	3.5 (1.8, 4.1)	4.0 (2.1, 5.2)	0.19	0.079	3.0 (1.8, 4.1)	2.6 (1.5, 3.5)	0.71	0.019
Troponin I, mcg/L	4.2 (1.2, 5.2)	4.0 (1.0, 4.8)	0.29	0.068	4.6 (1.2, 5.4)	5.6 (1.3, 6.3)	0.20	0.024
Interleukin-6, pg/mL	60.2 (25.5, 119.2)	71.0 (26.3, 121.0)	0.11	0.073	70.5 (30.5, 125.0)	86.1 (33.2, 126.5)	0.11	0.087
C-Reactive protein, mg/L	87.2 (41.5, 103.5)	89.4 (43.2, 109.0)	0.71	0.022	82.1 (41.2, 103.3)	78.4 (39.5, 99.8)	0.71	0.030
Procalcitonin, ng/mL	0.6 (0.2, 0.9)	0.9 (0.3, 1.4)	0.13	0.055	0.4 (0.2, 0.8)	0.6 (0.2, 0.9)	0.71	0.021
D-Dimer, ng/ml	1117.0 (544.0, 2010.5)	999.0 (510.2, 1816.5)	0.32	0.082	1465.5 (616.5, 2191.5)	1592.1 (710.5, 2548.0)	0.30	0.020
In-hospital statins	59 (30.1%)	49 (25.0%)	0.20	0.069	72 (30.5%)	55 (23.3%)	0.11	0.090
In-hospital antiplatelet	50 (25.5%)	49 (25.0%)	0.77	0.029	59 (25.0%)	50 (21.2%)	0.31	0.079
In-hospital anticoagulant	178 (90.8%)	177 (90.3%)	0.70	0.030	214 (90.7%)	212 (89.8%)	0.41	0.031
In-hospital hydroxychloroquine	147 (75.0%)	141 (71.9%)	0.15	0.084	177 (75.0%)	171 (72.5%)	0.50	0.030
In-hospital chloroquine	5 (2.6%)	8 (4.1%)	0.09	0.079	4 (1.7%)	5 (2.2%)	0.77	0.042
In-hospital lopinavir/ritonavir	83 (42.3%)	80 (40.8%)	0.41	0.047	99 (41.9%)	85 (36.0%)	0.14	0.076
In-hospital azithromycin	104 (53.1%)	104 (53.1%)	0.81	0.011	119 (50.4%)	116 (49.2%)	0.65	0.029
In-hospital remdesivir	4 (2.0%)	2 (1.0%)	0.17	0.092	2 (0.8%)	1 (0.4%)	0.73	0.093
In-hospital interferon- β	22 (11.2%)	21 (10.7%)	0.41	0.078	20 (8.5%)	14 (5.9%)	0.19	0.051
In-hospital corticosteroids	80 (40.8%)	81 (41.3%)	0.82	0.024	97 (41.1%)	96 (40.7%)	0.71	0.027
In-hospital tocilizumab	12 (6.1%)	10 (5.1%)	0.27	0.068	10 (4.2%)	8 (3.4%)	0.23	0.059
	RAASi withdrawal (n=178)	Non-RAASi use (n=178)	<i>P</i> value	SMD				
Age (years)	80.9 \pm 10.0	81.8 \pm 10.8	0.18	0.024				
Male gender	89 (50.0%)	94 (52.8%)	0.29	0.041				
History of smoking	66 (37.1%)	61 (34.3%)	0.28	0.044				
Obesity	45 (25.3%)	39 (21.9%)	0.16	0.067				

Diabetes mellitus	62 (34.8%)	59 (33.1%)	0.42	0.020
Hypertension	144 (80.9%)	132 (74.2%)	0.22	0.069
Dyslipidemia	98 (55.1%)	92 (51.7%)	0.29	0.077
Chronic kidney disease	36 (20.2%)	35 (19.7%)	0.61	0.038
Atrial fibrillation	87 (48.9%)	88 (49.4%)	0.60	0.033
Coronary artery disease	76 (42.7%)	70 (39.3%)	0.25	0.054
Chronic obstructive pulmonary disease	31 (17.4%)	30 (16.9%)	0.59	0.031
Stroke	13 (7.3%)	11(6.2%)	0.27	0.076
Dementia	36 (20.2%)	40 (22.5%)	0.32	0.059
Moderate-severe functional dependence	71 (40.0%)	81 (45.5%)	0.18	0.081
Moderate-severe comorbidity	174 (97.8%)	175 (98.3%)	0.71	0.021
Statins	81 (45.5%)	72 (40.4%)	0.18	0.080
Antiplatelet	53 (29.8%)	48 (27.0%)	0.29	0.049
Anticoagulant	79 (44.4%)	82 (46.1%)	0.22	0.083
Disease severity				
Moderate	118 (66.3%)	117 (65.7%)	0.31	0.052
Severe	52 (29.2%)	53 (29.8)		
Critical	8 (4.5%)	8 (4.5%)		
Blood glucose, mg/dL	148.3 ± 70.2	141.5 ± 68.9	0.18	0.061
Creatinine, md/dL	1.2 (0.9, 1.7)	1.2 (0.9, 1.7)	0.90	0.021
Blood urea nitrogen, mg/dL	61 (48, 97)	60 (47, 92)	0.31	0.052
Ferritin, mcg/L	625.2 (268.0, 1115.5)	775.1 (365.1, 1666.0)	0.18	0.083
Lactate, mmol/L	3.9 (2.0, 5.0)	2.9 (1.6, 3.8)	0.20	0.080
Troponin I, mcg/L	4.2 (1.1, 4.9)	5.5 (1.4, 6.0)	0.18	0.074
Interleukin-6, pg/mL	90.5 (29.9, 131.5)	100.5 (35.8, 134.5)	0.26	0.066
C-Reactive protein, mg/L	90.0 (42.0, 109.1)	85.2 (37.9, 100.7)	0.36	0.065
Procalcitonin, ng/mL	1.0 (0.3, 1.5)	0.9 (0.2, 1.3)	0.19	0.071
D-Dimer, ng/ml	1236.0 (612.0, 2108.4)	1395.5 (712.4, 2777.5)	0.16	0.090
In-hospital statins	30 (16.9%)	30 (16.9%)	0.71	0.026
In-hospital antiplatelet	39 (21.9%)	36 (20.2%)	0.29	0.022
In-hospital anticoagulant	160 (90.0%)	159 (89.3%)	0.63	0.030
In-hospital hydroxychloroquine	128 (71.9%)	129 (72.5%)	0.58	0.033

In-hospital chloroquine	6 (3.4%)	4 (2.2%)	0.69	0.035
In-hospital lopinavir/ritonavir	66 (37.1%)	63 (35.4%)	0.18	0.062
In-hospital azithromycin	91 (51.1%)	89 (50.0%)	0.39	0.040
In-hospital remdesivir	1 (0.5%)	1 (0.5%)	0.58	0.093
In-hospital interferon- β	14 (7.9%)	10 (5.6%)	0.30	0.088
In-hospital corticosteroids	74 (41.2%)	72 (40.4%)	0.63	0.079
In-hospital tocilizumab	7 (3.9%)	6 (3.4%)	0.40	0.088

Data are shown as mean (standard deviations) or median (first quartile, third quartile) when they did not show a normal distribution, absolute values, and percentages. A significant imbalance was considered if a standardized mean difference between baseline variables of greater than 10%. Values were considered to be statistically significant when $P < 0.05$.

Only principal characteristics of patients are shown.

SMD: standardized mean difference