

Supplementary Material

Quantifying Renin-Angiotensin-System Alterations in COVID-19

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Table 1. Mean RAS peptide levels and enzymatic activities collected from different studies.

	Unit	Severe	Non-Severe	Controls	<i>p</i> -value	<i>N</i>	Method	Ref
ACE activity	U/mL	49 [37–68]	64 [52–78]	75 [58–99]	<0.001	196	KPSM	[1]
	U/mL	44 [32–53]	48 [36–55]	35 [25–51]	0.01	96	ELISA	[2]
	RFU/nL	0.22 [0.27–0.18]	0.2 [0.3–0.16]	0.3 [0.35–0.24]	-	33	FA	[3]
ACE level	ng/mL	57 [45–70]		64 [48–265]	-	124	ELISA	[4]
ACE2 activity	RFU/nL	0.15 [0.2–0.09]	0.16 [0.2–0.11]	0.13 [0.16–0.1]	-	33	FA	[3]
	pmol/min/mL	11.2 [8.3–22]	5.4 [1.8–9.0]	0.06 [0.02–2.2]	<0.0001	136	FA	[5]
POP activity	RFU/nL	0.09 [0.13–0.06]	0.12 [0.07–0.17]	0.08 [0.12–0.05]	-	33	FA	[3]
ACE2 level	ng/mL	8.5 [4.7–10.6]		0.8 [0.7–1.0]	<0.001	15	LC-MS	[6]
	ng/mL	2.1 [1.3–3.0]	1.3 [1.0–2.4]	-	-	153	LC-MS	[7]
	ng/mL	15.1 [9.8–32]	3.2 [1.8–4.7]	-	<0.001	153	LC-MS	[7]
	ng/mL	19.4 [±2]		22.6 [±4]	<0.05	45	ELISA	[8]
	ng/mL	5.0 [2.8–11.8]		1.4 [1.1–1.6]	<0.0001	124	ELISA	[4]
	NPX	1.5 [1.0–2.4]	1.1 [0.9–1.6]		<0.001	205	PEA	[9]
	NPX	4 [2.4–5.0]	1.8 [1.5–2.4]		<0.0001	205	PEA	[9]
	ng/mL	1.4 [0.7–3.5]	2.1 [0.6–22.4]	0.5 [0.1–1.9]	0.001	96	ELISA	[2]
	ng/mL	1.3 [±0.1]	1.5 [±0.1]	-	<0.01	85	ELISA	[10]
	ng/mL	94 [46–300]		43 [37–95]	-	15	LC-MS	[6]
AngI level	ng/mL	31 [±6]		41 [±] 10	-	38	LC-MS	[11]
	ng/mL	1.5 [1.3–2.0]		3.3 [2.0–4.0]	<0.005	45	ELISA	[8]
	ng/mL	0.4 [0.4–0.5]	1.0 [0.6–1.5]	-	0.03	28	ELISA	[12]
	pg/mL	42 [32–45]	39 [26–47]	37 [24–47]	-	96	ELISA	[2]
	ng/mL	0.15 [0.1–0.22]		0.7 [0.5–1.0]	<0.001	41	ELISA	[13]
AngII level	ng/mL	52 [30–78]		137 [105–495]	0.008	15	LC-MS	[6]
	pmol/L	166 [61–680]	48 [16–131]	-	<0.01	153	LC-MS	[7]
	pmol/L	96 [38–250]	33 [9–78]	-	<0.01	153	LC-MS	[7]
	ng/mL	6.0 [±1.1]		10.7 [±1.9]	<0.05	38	LC-MS	[11]
	ng/mL	1.0 [0.7–1.3]		0.7 [0.4–1.1]	<0.05	45	ELISA	[8]
	ng/mL	0.25 [0.2–0.3]	0.6 [0.25–0.9]	-	0.04	28	ELISA	[12]
	ng/mL	0.21 [0.13–0.42]		0.13 [0.08–0.17]	<0.01	27	ELISA	[14]
	pg/mL	56 [23–131]	99 [65–153]	103 [71–140]	-	94	ELISA	[2]
	ng/mL	0.15 [0.13–0.17]	0.13 [0.12–0.16]	-	<0.01	55	ELISA	[15]
	ng/mL	0.4 [0.2–3.0]		0.8 [0.3–4.8]	<0.001	112	ELISA	[16]
	ng/mL	4.8 [4.4–5.2]		4.4 [4.2–4.6]	<0.01	85	ELISA	[10]
Ang1–7 level	pmol/L	25 [14–35]	18 [11–25]	17 [8–25]	-	33	RIA	[3]
	ng/mL	24 [5.4–40]		2.0 [2.0–3.3]	0.004	15	LC-MS	[6]
	pmol/L	11 [5–51]	1.5 [1.5–5.0]	-	<0.001	153	LC-MS	[7]
	pmol/L	50 [15–132]	1.5 [1.5–3.7]	-	<0.001	153	LC-MS	[7]
	ng/mL	14 [±2.3]		7.5 [±1.4]	<0.05	38	LC-MS	[11]
	ng/mL	0.5 [0.4–0.7]		0.5 [0.4–0.6]	-	45	ELISA	[8]
	ng/mL	0.2 [0.2–0.3]	0.3 [0.2–0.4]	-	0.04	28	ELISA	[12]
	pg/mL	14.3 [1.6–33]	8.4 [2.8–28]	0.98 [0.98–3.7]	<0.001	96	ELISA	[2]
	ng/mL	0.17 [0.13–0.27]		0.32 [0.22–0.37]	0.003	41	ELISA	[13]
	pmol/L	15 [0–60]	17 [0–70]	10 [5–15]	-	33	RIA	[3]
Ang1–5 level	ng/mL	9.0 [5.7–14]		4.3 [2.6–14]	-	15	LC-MS	[6]
	ng/mL	3.4 [±0.8]		19.3 [±6.3]	<0.01	38	LC-MS	[11]

The values for three classes of individuals (severe COVID-19, non-severe COVID-19 and controls) or two classes (COVID-19 and controls) are reported. *N* is the number of samples on which the experimental measures have been done. The different experimental methods used in the measurements of the peptide levels are: liquid chromatography-mass spectrometry (LC-MS), enzyme-linked immunosorbent assay (ELISA), kinetic spectrophotometry (KPSM), fluorescence assay

(FA), radioimmunoassay (RIA) and proximity extension assay (PEA). Only the *p*-values reported by the authors to be statistically significant (<0.05) are shown.

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