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Supplemental figures and tables

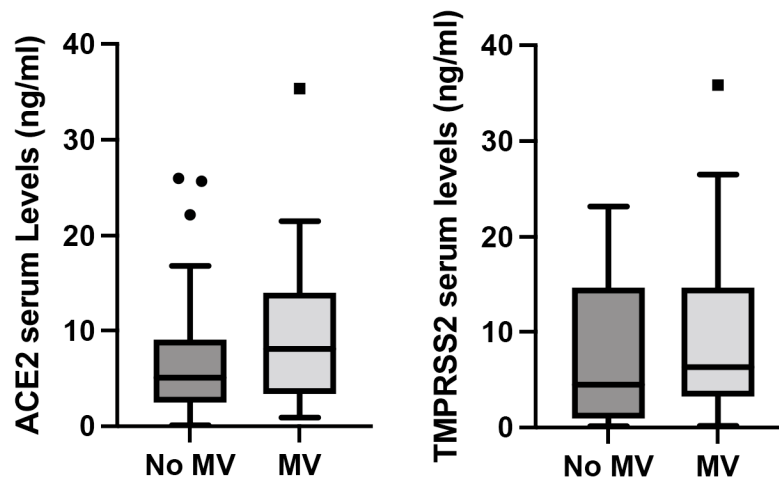


Figure S1. ACE2 and TMPRSS2 serum levels at presentation for patients who ultimately required mechanical ventilation (MV) and those who did not (no MV).

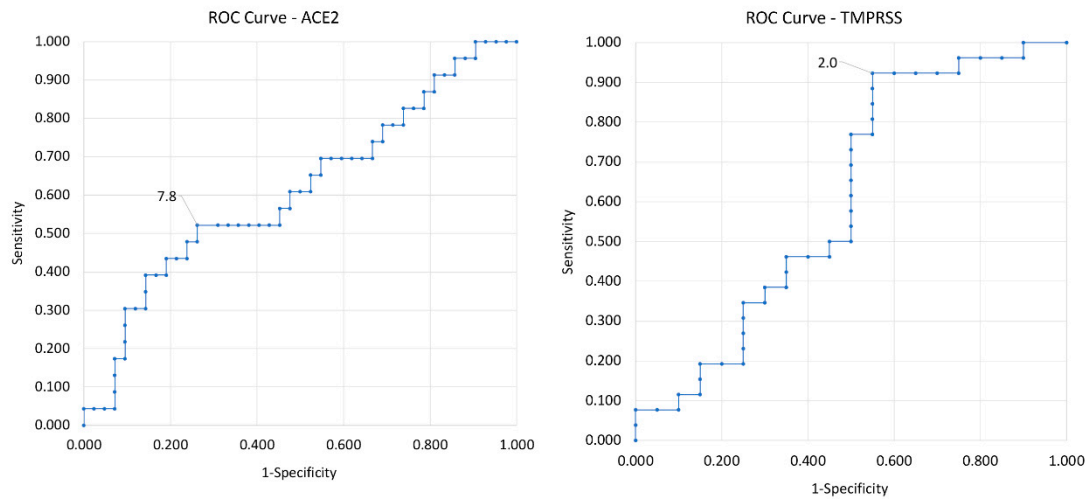


Figure S2. ROC curves for ACE2 and TMPRSS2 levels early in COVID-19 for correlation with need for mechanical ventilation. ROC analysis dichotomized ACE2 levels in order to predict the risk for requiring mechanical ventilation. ACE2 levels that produced the highest sensitivity & specificity for predicting the need for mechanical ventilation was above 7.8ng/mL. For TMPRSS2, expression levels that produced the highest sensitivity & specificity for predicting the need for mechanical ventilation was above 2ng/mL.

Table S1. Association between early sample ACE2 or TMPRSS2 serum expression and clinical characteristics in COVID-19 patients

Variable		ACE2	p-value	TMPRSS2	p-value
Hypertension	Yes	6.24 (2.92-12.39)	0.602	6.93 (2.13-15.13)	0.698
	No	5.59 (3.60-9.99)		5.52 (2.59-13.55)	
Diabetes	Yes	6.60 (3.50-12.56)	0.446	6.07 (2.07-15.62)	0.572
	No	5.27 (2.44-10.01)		5.81 (2.24-13.95)	
Dyslipidemia	Yes	9.15 (5.66-15.80)	0.002	8.34 (3.73-16.28)	0.099
	No	4.13 (2.45-7.95)		4.75 (1.80-13.62)	
Sex	Female	5.27 (3.06-12.11)	0.976	3.58 (1.04-14.10)	0.549
	Male	5.67 (3.01-10.13)		6.33 (2.43-14.46)	

Table S2. Clinical outcomes in COVID-19 patients who required mechanical ventilation compared to those who did not

	Non-ventilation n=42 n (%)	Ventilation n=30 n (%)	p value
Mortality	4 (9.5%)	11 (36.7%)	0.005
Hospitalization >7 days	20 (47.6%)	30 (100.0%)	<0.001
Inotropic support	0 (0.0%)	29 (96.7%)	< 0.001
Acute renal failure*	7 (16.7%)	17 (58.6%)	< 0.001
RRT	0 (0.0%)	10 (33.3%)	< 0.001
ECMO	0 (0.0%)	8 (26.7%)	< 0.001
Blood products	5 (11.9%)	20 (66.7%)	< 0.001
DIC	0 (0.0%)	3 (10.0%)	0.036
PE/DVT	1 (2.4%)	7 (23.3%)	0.005
HIT	0 (0.0%)	3 (10.0%)	0.036
Bleeding	1 (2.4%)	18 (60.0%)	< 0.001
Pneumothorax	0 (0.0%)	3 (10.0%)	0.036
Sepsis	2 (4.8%)	26 (86.7%)	< 0.001

*Acute renal failure – increase in creatinine from baseline in 50%.

DIC, Disseminated intravascular coagulation; DVT, Deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; HIT, Heparin-induced thrombocytopenia; PE, Pulmonary embolism; RRT, renal replacement therapy.

Table S3. Laboratory results in COVID-19 patients who required mechanical ventilation and those who did not

	No mechanical ventilation N=42	Mechanical ventilation N=30	p value
Creatinine mg\dl (Max) (N=72)	0.98 (0.80-1.77)	1.81 (1.07-3.44)	0.003
WBC K\micl (N=71)	5.62 (4.59-7.27)	8.75 (6.53-13.84)	0.002
WBC K\micl (Min) (N=71)	5.19±1.82	5.45±2.12	0.516
WBC K\micl (Max) (N=71)	8.19 (5.95-11.30)	19.98 (13.96-33.20)	<0.001
% Lympho (N=71)	16.45 (14.15-21.30)	9.90 (6.30-15.80)	0.005
Hb g\dl (Min) (N=72)	12.22 (9.83-13.09)	7.08 (6.78-8.26)	<0.001
PLT K\micl (Min) (N=72)	161.5 (144.5-192)	118.5 (67.2-164.7)	0.005
CRP g\dl (N=71)	70.8 (24.6-126.6)	114.9 (70.5-243.5)	0.013
CRP g\dl (Max) (N=72)	107.8 (67.4-210.2)	329.7 (285.0-401.0)	<0.001
PCT µg\l (N=41)	0.83 (0.47-1.79)	0.47 (0.32-0.92)	0.147
PCT µg\l (Max) (N=47)	1.09 (0.54-3.28)	4.56 (1.88-14.27)	0.004
ALT U\l (N=71)	24.5 (17-32.7)	41.0 (27.0-58.0)	<0.001
AST U\l (N=71)	35.5 (28.2-50.5)	60.0 (42.0-95.0)	<0.001
LDH U\l (N=71)	288.5 (227.2-398.0)	449.0 (357.0-676.0)	<0.001
Triglycerides mg\dl (N=38)	148.0 (113.5-185.8)	187.0 (143.8-289.0)	0.035
Troponin ng\ml (N=66)	9.5 (4.7-13.7)	13.2 (9.8-36.5)	0.015
D-dimer ng\ml (N=62)	695.0 (495.0-1200.0)	1425.5 (649.5-3682.5)	0.021
D-dimer max ng\ml (N=69)	1007.0 (573.2-5569.8)	22726 (8195-47938)	<0.001
Fibrinogen mg\dl (Min) (N=61)	439.35±170.39	231.83±131	<0.001
CPK U\l (N=42)	106.5 (61.0-227.0)	162.5 (64.0-272.2)	0.930
TNF pg\ml (N=15)	22 (17-38.2)	28 (24.5-38)	0.571
TNF pg\ml (Max) (N=31)	29.5±22.27	31.44±12.43	0.844
IL8 pg\ml (N=15)	105 (81-262.2)	52 (33-94.5)	0.104
IL8 pg\ml (Max) (N=31)	75 (36.7-114)	56 (43-97)	0.783
IL 1B pg\ml (N=15)	0.5 (0.0-1.0)	1.0 (0.0-1.0)	0.721
IL 1B pg\ml (Max) (N=31)	0.00 (0.00-0.75)	1.00 (0.00-1.00)	0.383
IL6 pg\ml (N=15)	48.0 (34.7-65.5)	186.0 (79.0-369.0)	0.078
IL6 pg\ml (Max) (N=32)	36.0 (26.5-60.5)	193.0 (86.0-657.0)	0.001

Mean±SD; values upon admission if not stated otherwise. Abbreviations: WBC – White blood count, Lympho - Lymphocytes, Hb – Hemoglobin, PLT – Platelets, CRP - C-reactive protein, PCT – Procalcitonin, ALP - Alkaline Phosphatase, GGT - Gamma Glutamyl Transpeptidase, ALT - Alanine transaminase, AST - Aspartate Aminotransferase, LDH - Lactate Dehydrogenase, CPK - creatine phosphokinase, TNF - Tumor necrosis factor, IL8 - Interleukin 8, IL-1B - interleukin 1, beta, IL 6 - Interleukin 6

Table S4. Correlations between ACE2 and other biomarkers associated with disease severity in COVID-19

Variables Correlated with ACE2	Correlation Coefficient	p value
Creatinine mg\dl (Max) (N=65)	-0.018	0.886
WBC K\micl (N=64)	0.379	0.002
WBC K\micl (Min) (N=64)	0.378	0.002
WBC K\micl (Max) (N=64)	0.271	0.031
% Lympho (N=64)	-0.414	<0.001
Hb g\dl (Min) (N=65)	-0.118	0.349
PLT K\micl (Min) (N=65)	0.259	0.037
CRP g\dl (N=64)	0.494	<0.001
CRP g\dl (Max) (N=65)	0.302	0.014
PCT µg\l (N=35)	0.465	0.005
PCT µg\l (Max) (N=40)	0.348	0.028
ALT U\l (N=64)	0.296	0.018
AST U\l (N=64)	0.310	0.013
LDH U\l (N=64)	0.457	<0.001
Triglycerides mg\dl (N=34)	0.245	0.162
Troponin ng\ml (N=60)	0.229	0.078
D-dimer ng\ml (N=56)	0.470	<0.001
D-dimer max ng\ml (N=62)	0.293	0.021
Fibrinogen mg\dl (Min) (N=54)	-0.015	0.912
CPK U\l (N=40)	-0.093	0.566
TNF pg\ml (N=14)	0.312	0.277
TNF pg\ml (Max) (N=26)	0.196	0.337
IL8 pg\ml (N=14)	-0.081	0.785
IL8 pg\ml (Max) (N=26)	0.093	0.650
IL 1B pg\ml (N=14)	0.178	0.542
IL 1B pg\ml (Max) (N=26)	0.204	0.317
IL6 pg\ml (N=14)	0.147	0.616
IL6 pg\ml (Max) (N=27)	0.273	0.168

Table S5. *TMPRSS2* at an early disease stage is not an independent predictor of mechanical ventilation in COVID-19

	OR	95% CI	P-value
TMPRSS1 (Above 2 vs Below 2)	4.626	0.393-54.414	0.223
Age	0.828	0.728-0.941	0.004
Gender (Male vs Female)	1.819	0.163-20.261	0.626
Acute renal failure*	38.920	2.809-539.37	0.006

*Acute renal failure – increase in creatinine from baseline in 50%

Abbreviations: OR = odds ratio, CI = confidence interval, ACE2 - Angiotensin converting enzyme 2

Table S6. ACE2 and TMPRSS2 serum levels late in the disease course in COVID-19 patients

	ACE2 – second sample		p value	TMPRSS2 – second sample		p value
	No mean±SD (n)	Yes mean±SD (n)		No mean±SD (n)	Yes mean±SD (n)	
MV*	8.85 (4.23- 11.92) (9)	11.54 (8.00- 14.41) (21)	0.298	1.97 (0.54- 4.03) (9)	6.53 (2.66- 20.11) (21)	0.045
LOS >7 days		10.05 (7.60- 13.81) (30)	NA		4.46 (1.32- 9.96) (30)	NA
CCCU stay	8.85 (4.23- 11.92) (9)	11.5 (8.00- 14.41) (21)	0.298	1.97 (0.54- 4.03) (12)	6.53 (2.66- 20.11) (18)	0.045
Sepsis	9.0 (4.13- 13.59) (12)	10.98 (8.12- 13.72) (18)	0.626	3.79 (0.54- 6.67) (15)	5.67 (1.69- 18.57) (15)	0.249
AKI*	11.92 (8.24- 13.86) (15)	9.67 (5.64- 13.21) (15)	0.507	4.80 (1.26- 13.44) (21)	4.41 (1.34- 6.77) (9)	0.806
CVVH	10.42 (8.09- 14.41) (21)	9.67 (3.82- 12.45) (9)	0.342	4.80 (1.97- 10.5) (25)	2.66 (0.94- 7.01) (5)	0.449
Dialysis	9.59 (7.47- 14.41) (25)	11.54 (9.67- 12.45) (5)	0.978	4.51 (1.97- 8.34) (25)	1.37 (0.28- 21.98) (5)	0.666
ECMO	11.54 (8.47- 14.41) (25)	7.47 (3.82- 8.00) (5)	0.101	4.03 (1.31- 10.5) (20)	7.01 (4.41- 7.61) (10)	0.589
Mortality	11.73 (8.66- 14.59) (20)	8.24 (4.73- 11.76) (10)	0.159	5.10 (1.80- 20.58) (20)	2.94 (1.04- 6.00) (10)	0.120

*MV – Mechanical Ventilation; AKI - Acute renal failure – increase in creatinine from baseline in 50%, Abbreviations: ACE2 – Angiotensin converting enzyme 2, TMPRSS2 - transmembrane serine protease 2, ARF – acute renal failure, ECMO – extracorporeal membrane oxygenation, LOS – length of stay, mechanically ventilated, CVVH – continuous veno-venous hemofiltration.

Table S7. *ACE2/TMPRSS2* ratio does not predict the risk for mechanical ventilation in COVID-19 patients

Outcomes		ACE2/TMPRSS2 Ratio	p-value
Intubated	Yes	0.84 (0.34-2.46)	0.477
	No	1.08 (0.68-5.35)	
AKI	Yes	1.19 (0.47-9.29)	0.261
	No	0.91 (0.34-2.05)	
Dialysis/CVVH	Yes	2.07 (0.76-7.87)	0.248
	No	1.03 (0.34-2.37)	
CCCU Admission	Yes	0.90 (0.34-2.75)	0.671
	No	1.04 (0.58-4.75)	