Supplemental Material

Tables

Table S1. Receiving Operating Characteristic (ROC) curve analysis by Brown–Wilson test for ICU admission in patients with severe COVID-19 pneumonia using isolated values of BK1-8, BK and D-dimer and the multivariate model score

Variables	ROC analysis by Brown-Wilson Test			
	A.U.C.	**95% C.I.**	***P*-value**	**Youden cut-off value (sensitivity, specificity)**
BK1-8	0.770	0.620 to 0.920	0.0011	8.201 ng/mL (58.8%, 93.48%)
BK	0.734	0.610 to 0.858	0.0047	31.17 pg/mL (88.24%, 60.0%)
D-dimer	0.840	0.719 to 0.961	0.0002	1425 ng/mL (71.4%, 90.5%)
Multivariate model score	0.966	0.922 to 1.000	<0.0001	-0,3521 (92.9%, 95.2%)

A.U.C.: area under the curve, C.I.: confidence interval. *P*-value and Youden optimal cut-off value (including sensitivity and specificity) are shown.

Table S2 Multivariate logistic regression model including BK1-8, BK and D-dimer as independent determinants of ICU admission in patients with severe COVID-19 pneumonia

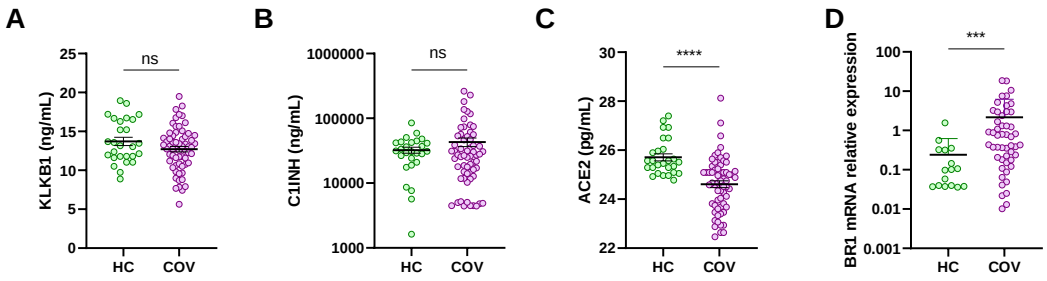
	B	**S.E.**	**Wald**	**p-Value**	**Exp(B)**	**95.0% C.I. for EXP(B)**	
						Lower	Upper
BK1-8	0.709	2.52	7.913	0.005	2.032	1.240	3.329
BK	-0.044	0.045	0.919	0.338	0.957	0.876	1.047
D-dimer	0.001	0.000	6.353	0.012	1.001	1.000	1.002
Constant	-7.444	2.376	9.821	0.002	0.001		

S.E.: standard error, C.I.: confidence interval.

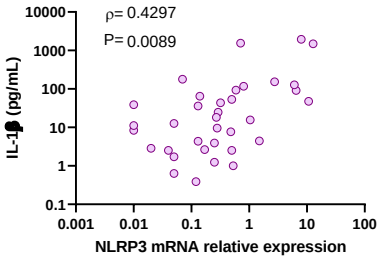
Table S3. ELISA kits used in the study

ELISA target	Manufacturer	Reference	Detection limit
HK	CUSABIO technology, USA	CSB-EL012479HU	47 ng/mL
BK	Cloud-Clone Corp., USA	CEA874Hu	0.51 pg/mL
BK1-8	MyBioSource, USA	MBS109439	0.1 ng/mL
CPN1	Cloud-Clone Corp., USA	SEF323Hu	6.7 pg/mL
KLKB1	FineTest, China	EH14758	0.375 ng/mL
C1INH	FineTest, China	EH2726	1.875 ng/mL
ACE2	Cloud-Clone Corp., USA	SEB886Hu	5.5 pg/mL
TF	CUSABIO technology, USA	CSB-E07913h	3.12 pg/mL
CD40L	Invitrogen, Austria	BMS293	0.06 ng/mL
GSDMD	MyBioSource, USA	MBS2705515	0.312 ng/mL

Figures



Supplemental Figure S1. Kallikrein-kinin proteins quantification in plasma. (A) ELISA quantification of KLKB1 concentration in plasma from HC (n=27) and COVID-19 patients (N=63). **(B)** ELISA quantification of C1INH concentration in plasma from HC (n=27) and COVID-19 patients (N=62). **(C)** ELISA quantification of ACE2 concentration in plasma from HC (n=27) and COVID-19 patients (N=63). **(D)** Relative BR1 mRNA expression in circulating cells from HC (n=16) and COVID-19 patients (n=50). Mean differences were analysed by Mann-Whitney U test. Error bars: mean ± SEM. ns: non-significant; ***: $P<0.001$; ****: $P<0.0001$.



Supplemental Figure S2. **NLRP3 correlates with IL-1β**. Correlation of NLRP3 mRNA expression in PBMCs and IL-1β plasma concentration from COVID-19 patients (n=36). Spearman's correlation coefficient (ρ) and P-value are shown.