

SUPPLEMENTAL FILE

Neutrophil Extracellular Traps and Platelet Activation for Identifying Severe Episodes and Clinical Trajectories in COVID-19

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Table S1. Biomarker levels and demographics.

	Age ≤ 65 years (N=114)	Age > 65 years (N=90)	P
CitH3 (AU)	0.071 [0.064, 0.082]	0.077 [0.067, 0.089]	0.027
cfDNA (ng/uL)	2997 [2574, 3840]	3334 [2802, 3887]	0.122
sCD40L (ng/mL)	1.33 [0.84, 1.78]	1.25 [0.81, 1.94]	0.877
sP-selectin (ng/mL)	5.76 [4.51, 7.20]	6.63 [4.49, 8.97]	0.031
	Female (N=95)	Male (N=109)	P
CitH3 (AU)	0.071 [0.063, 0.079]	0.076 [0.066, 0.088]	0.022
cfDNA (ng/uL)	2958 [2571, 3739]	3362 [2841, 4084]	0.004
sCD40L (ng/mL)	1.26 [0.93, 2.04]	1.30 [0.80, 1.82]	0.627
sP-selectin (ng/mL)	5.89 [4.49, 7.29]	5.92 [4.51, 7.89]	0.475

Data is summarised as median [1st quartile, 3rd quartile].

Table S2. Biomarker levels and comorbidities.

	No Chronic Heart Disease (N=179)	Chronic Heart Disease (N=25)	P
CitH3 (AU)	0.073 [0.064, 0.085]	0.073 [0.066, 0.079]	0.769
cfDNA (ng/uL)	3152 [2689, 3840]	3143 [2781, 4055]	0.739
sCD40L (ng/mL)	1.30 [0.84, 1.93]	1.11 [0.68, 1.93]	0.469
sP-selectin (ng/mL)	5.91 [4.49, 7.63]	6.26 [4.72, 8.61]	0.439
	No Diabetes (N=158)	Diabetes (N=46)	P
CitH3 (AU)	0.073 [0.064, 0.085]	0.074 [0.065, 0.082]	0.506
cfDNA (ng/uL)	3053 [2669, 3754]	3505 [2805, 4075]	0.147
sCD40L (ng/mL)	1.24 [0.80, 1.68]	1.49 [0.99, 2.21]	0.016
sP-selectin (ng/mL)	5.89 [4.49, 7.54]	6.39 [4.51, 7.89]	0.332
	No Hypertension (N=118)	Hypertension (N=86)	P
CitH3 (AU)	0.071 [0.064, 0.081]	0.077 [0.066, 0.089]	0.045
cfDNA (ng/uL)	2981 [2654, 3840]	3328 [2802, 3948]	0.177
sCD40L (ng/mL)	1.29 [0.84, 1.77]	1.27 [0.81, 1.98]	0.845
sP-selectin (ng/mL)	5.79 [4.46, 7.54]	6.23 [4.73, 8.47]	0.137
	No Dyslipidemia (N=142)	Dyslipidemia (N=62)	P
CitH3 (AU)	0.073 [0.064, 0.084]	0.073 [0.065, 0.086]	0.769
cfDNA (ng/uL)	3056 [2656, 3829]	3350 [2781, 4045]	0.191
sCD40L (ng/mL)	1.26 [0.87, 1.93]	1.32 [0.80, 1.82]	0.713
sP-selectin (ng/mL)	5.91 [4.49, 7.56]	6.03 [4.65, 8.71]	0.431

Data is summarised as median [1st quartile, 3rd quartile].

Table S3. Biomarker levels and clinical outcomes

	No Mortality (N=178)	Mortality (N=26)	P
CitH3 (AU)	0.073 [0.064, 0.082]	0.080 [0.067, 0.095]	0.131
cfDNA (ng/uL)	3056 [2656, 3753]	3764 [3038, 5004]	0.002
sCD40L (ng/mL)	1.29 [0.84, 1.82]	1.23 [0.72, 1.99]	0.572
sP-selectin (ng/mL)	5.91 [4.51, 7.63]	6.1 [4.49, 7.8]	0.849
	No supplemental oxygen (N=104)	Supplemental oxygen (N=100)	P
CitH3 (AU)	0.071 [0.064, 0.078]	0.077 [0.067, 0.091]	0.003
cfDNA (ng/uL)	2848 [2555, 3451]	3608 [2968, 4260]	<0.001
sCD40L (ng/mL)	1.33 [0.81, 2.08]	1.25 [0.86, 1.75]	0.575
sP-selectin (ng/mL)	5.72 [4.49, 7.26]	6.28 [4.58, 7.91]	0.388
	No radiological progression (N=131)	Radiological progression (N=73)	P
CitH3 (AU)	0.072 [0.064, 0.082]	0.076 [0.067, 0.090]	0.054
cfDNA (ng/uL)	2976 [2583, 3745]	3552 [2945, 4172]	<0.001
sCD40L (ng/mL)	1.32 [0.87, 2.15]	1.21 [0.72, 1.73]	0.125
sP-selectin (ng/mL)	5.87 [4.46, 7.54]	6.26 [4.67, 7.91]	0.537
	No respiratory support progression (N=133)	Respiratory support progression (N=71)	P
CitH3 (AU)	0.072 [0.064, 0.081]	0.075 [0.066, 0.095]	0.041
cfDNA (ng/uL)	2933 [2582, 3623]	3621 [2982, 4324]	<0.001
sCD40L (ng/mL)	1.34 [0.84, 2.05]	1.19 [0.81, 1.73]	0.232
sP-selectin (ng/mL)	5.72 [4.49, 7.23]	6.53 [4.67, 8.05]	0.145

Data is summarised as median [1st quartile, 3rd quartile].

Table S4. Area Under the Receiver Operating Characteristics Analysis.

Biomarker	Outpatients	ICU (first 24 h)	MV and/or death
CitH3	0.296 [0.199, 0.393]**	0.555 [0.286, 0.823]	0.608 [0.493, 0.722]*
cfDNA	0.247 [0.131, 0.362]***	0.904 [0.787, 1.000]***	0.744 [0.657, 0.831]***
sCD40L	0.479 [0.355, 0.603]	0.574 [0.372, 0.777]	0.477 [0.369, 0.584]
sP-selectin	0.408 [0.301, 0.515]	0.622 [0.407, 0.836]	0.546 [0.441, 0.651]

Data presented as AUROC [95% confidence interval]. AUROC denotes Area Under the Receiver Operating Characteristics; ICU: intensive care unit; MV: mechanical ventilation.

*p<0.05, **p<0.01, ***p<0.001

Table S5. Multistate model.

Biomarker	Transition	Hazard Ratio	95% Confidence Interval
CitH3	ED -> Discharge	0.64	[0.08, 1.06]
cfDNA	ED -> Discharge	0.50	[0.00, 1.22]
sCD40L	ED -> Discharge	1.01	[0.71, 1.51]
sP-selectin	ED -> Discharge	0.67	[0.26, 1.06]
CitH3	ED -> Ward	0.99	[0.81, 1.09]
cfDNA	ED -> Ward	0.99	[0.64, 1.17]
sCD40L	ED -> Ward	1.00	[0.95, 1.08]
sP-selectin	ED -> Ward	0.99	[0.78, 1.05]
CitH3	ED -> ICU	1.35	[1.05, 4.52]
cfDNA	ED -> ICU	1.59	[0.91, 2.99]
sCD40L	ED -> ICU	0.99	[0.44, 1.49]
sP-selectin	ED -> ICU	1.31	[1.03, 4.69]
CitH3	Ward -> Discharge	0.90	[0.62, 0.99]
cfDNA	Ward -> Discharge	0.84	[0.48, 0.99]
sCD40L	Ward -> Discharge	1.00	[0.92, 1.17]
sP-selectin	Ward -> Discharge	0.91	[0.75, 0.99]
CitH3	Ward -> ICU	1.00	[0.68, 1.21]
cfDNA	Ward -> ICU	1.00	[0.76, 1.34]
sCD40L	Ward -> ICU	1.00	[0.92, 1.11]
sP-selectin	Ward -> ICU	1.00	[0.79, 1.18]
CitH3	Ward -> Death	1.10	[0.99, 1.61]
cfDNA	Ward -> Death	1.16	[0.94, 2.02]
sCD40L	Ward -> Death	1.00	[0.84, 1.10]
sP-selectin	Ward -> Death	1.09	[1.00, 1.65]
CitH3	ICU -> Ward	0.36	[0.02, 1.21]
cfDNA	ICU -> Ward	0.20	[0.00, 1.22]
sCD40L	ICU -> Ward	1.01	[0.15, 16.10]
sP-selectin	ICU -> Ward	0.40	[0.00, 0.99]
CitH3	ICU -> Death	0.72	[0.00, 1.27]
cfDNA	ICU -> Death	0.59	[0.00, 1.42]
sCD40L	ICU -> Death	1.00	[0.53, 13.73]

sP-selectin	ICU -> Death	0.74	[0.00, 1.04]
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ED denotes emergency department; ICU: intensive care unit.

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Figure S1. Multistate model.