

Supplemental Material

Platelet activation and platelet-monocyte aggregates formation trigger tissue factor expression in severe COVID-19 patients

Running Title: Platelets drive monocyte TF expression in COVID-19

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Supplemental Table 1: Characteristics of COVID-19 patients admitted to the ICU based on the requirement of invasive mechanical ventilation or noninvasive oxygen supplementation.

Characteristics ¹	Noninvasive O ₂ Supplementation (N=8)	Mechanical ventilation (N=27)	p value ²
Age, years	48 (34 – 65)	58 (48 – 64)	0.3825
Sex, male	5 (62.5)	12 (44.4)	0.4430
SAPS 3	35 (29.5 – 46)	64 (58 – 73)	<0.0001
PaO ₂ /FiO ₂ ratio	483 (372 – 519)	141 (98 – 172)	0.0005
Vasopressor ³	0 (0 %)	16 (59.3 %)	0.0038
Time from symptom onset to blood sample, days	11 (8 – 15)	12 (8 – 17)	0.4178
28-day mortality	0 (0 %)	17 (63 %)	0.0029
Comorbidities			
Obesity	3 (37.5 %)	4 (14.8 %)	0.3117
Hypertension	4 (50 %)	14 (51.9 %)	1.0000
Diabetes	1 (12.5 %)	7 (25.9 %)	0.6478
Cancer	0 (0 %)	3 (11.1 %)	1.0000
Chronic heart disease	1 (12.5 %) ⁴	2 (7.4 %) ⁵	0.5531
Laboratory findings on admission			
Leukocytes, x 1000/μL	98 (35.5 – 110)	143 (104 – 210)	0.007
Lymphocytes, cells/μL	1269 (884 – 2343)	1136 (485 – 1556)	0.3180
Monocytes, cells/μL	495 (214 – 714.5)	712 (550 – 908)	0.1194
Platelets, x 1000/μL	223 (157 – 320.5)	193 (142.5 – 251)	0.5985
C Reactive Protein, mg/L	3.41 (0.73 – 14.04)	18.2 (7.9 – 26.13)	0.0105
Fibrinogen, mg/dL	426 (368 – 573)	545 (375 – 622)	0.5285
D-dimer, IU/mL	675 (371.5 – 2,359)	6,520 (3,337 – 17,065)	0.0001
IL-6, pg/mL	20.5 (11 – 256.8)	45 (20 – 86)	0.4337

¹Numerical variables are represented as the median and the interquartile range, and qualitative variables as the number and the percentage.

²The qualitative variables were compared using the two tailed Fisher exact test, and the numerical variables using the t test for parametric and the Mann Whitney U test for nonparametric distributions.

³Dopamine, epinephrine/norepinephrine, vasopressin or phenylephrine.

⁴Coronary artery disease.

⁵Congestive heart failure.

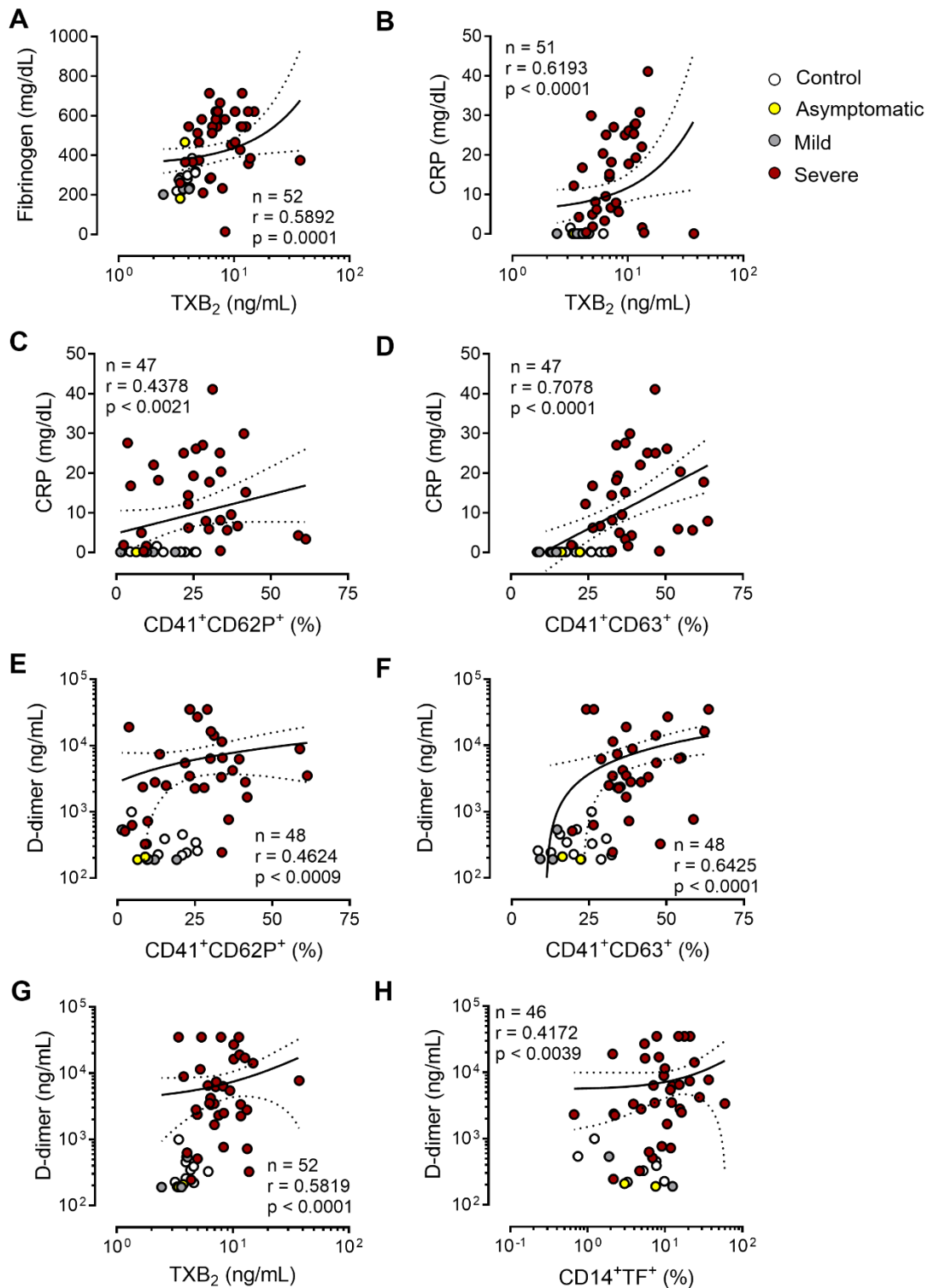
Supplemental Table 2: Characteristics of COVID-19 patients admitted to the ICU according to the 28-day mortality outcome as survivors or nonsurvivors.

Characteristics ¹	Survivors (N=18)	Nonsurvivors (N=17)	p value ²
Age, years	57 (40 – 63)	58 (52 – 73)	0.1722
Sex, male	7 (38.8 %)	10 (58.8 %)	0.3175
Respiratory support			
Mechanical ventilation	10 (55.6 %)	17 (100 %)	0.0029
SAPS 3	55.5 (37 – 64)	68 (59 – 78.5)	0.0024
PaO ₂ /FiO ₂ ratio	196 (155 – 429)	130 (87 – 150)	0.00114
Vasopressor ³	5 (27.8 %)	10 (58.8 %)	0.092
Time from symptom onset to blood sample, days	12 (9 – 17)	13 (8 – 18)	0.8330
Comorbidities			
Obesity	5 (27.8 %)	2 (11.8 %)	0.4018
Hypertension	9 (50 %)	9 (52.9 %)	1.0000
Diabetes	3 (16.7 %)	5 (29.4 %)	0.4430
Cancer	2 (11.1 %)	1 (5.9 %)	1.0000
Chronic heart disease	2 (11.1 %)	1 (5.9 %)	1.0000
Laboratory findings on admission			
Leukocytes, x 1000/ μ L	106 (76 – 140)	168 (122.5 – 268.5)	0.0024
Lymphocytes, cells/ μ L	1288 (939 – 1579)	1035 (283 – 1706)	0.5216
Monocytes, cells/ μ L	495 (214 – 715)	712 (550 – 9-8)	0.0097
Platelets, x 1000/ μ L	198 (154 – 324)	190 (136.8 – 233.5)	0.3455
C Reactive Protein, mg/L	7.29 (3.68 – 18.09)	20.3 (10.17 – 27.03)	0.0349
Fibrinogen, mg/dL	529 (366 – 582)	545 (402 – 622)	0.5943
D-dimer, IU/mL	2,436 (699 – 6,270)	7,731 (3,438 – 22,080)	0.0021
IL-6, pg/mL	21.5 (13.3 – 85.3)	56.25 (26 – 127.5)	0.0581

¹Numerical variables are represented as the median and the interquartile range, and qualitative variables as the number and the percentage.

²The qualitative variables were compared using the two tailed Fisher exact test, and the numerical variables using the t test for parametric and the Mann Whitney U test for nonparametric distributions.

³Dopamine, epinephrine/norepinephrine, vasopressin or phenylephrine.



Supplemental Figure 1: Platelet activation and monocyte TF expression associates with hyperinflammation and hypercoagulability in COVID-19. (A-B) The concentration of TXB₂ in plasma was plotted against the fibrinogen (A) and C reactive protein (B) levels. (C-D) The percentage of P-selectin (CD62P) (C) and CD63 (D) expression on platelets were plotted against the CRP concentration in plasma. (E-H) The percentage of P-selectin (CD62P) (E) and CD63 (F) expression on platelets, the concentration of TXB₂ in plasma (G) and the percentage of TF-expressing monocytes (H) were plotted against the D-dimer concentration in plasma. One outlier (CRP = 621.64 mg/dL) was excluded from the analysis in panels B-D according to the ROUT test. Linear regression (with the 95 % confidence interval) and Spearman's correlation were calculated according to the distribution of the dots.