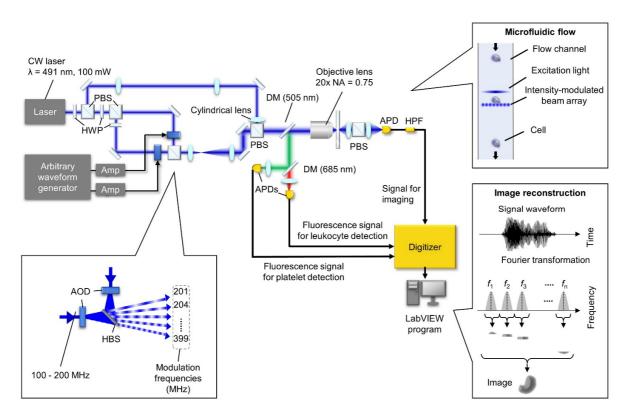
**Supplementary Information** 

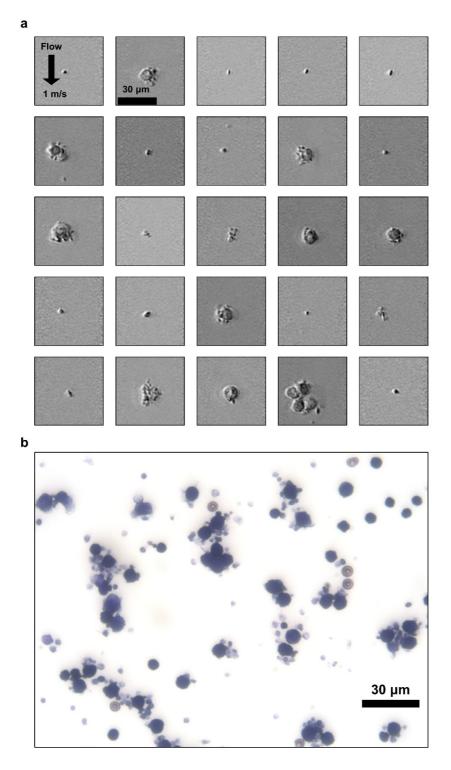
for

## Massive image-based single-cell profiling reveals high levels of circulating platelet aggregates in patients with COVID-19

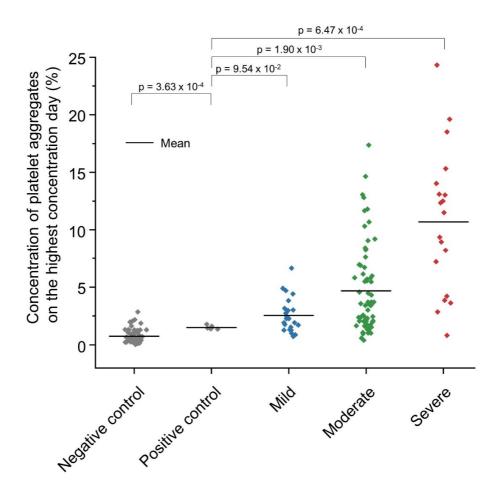
by Nishikawa et al.



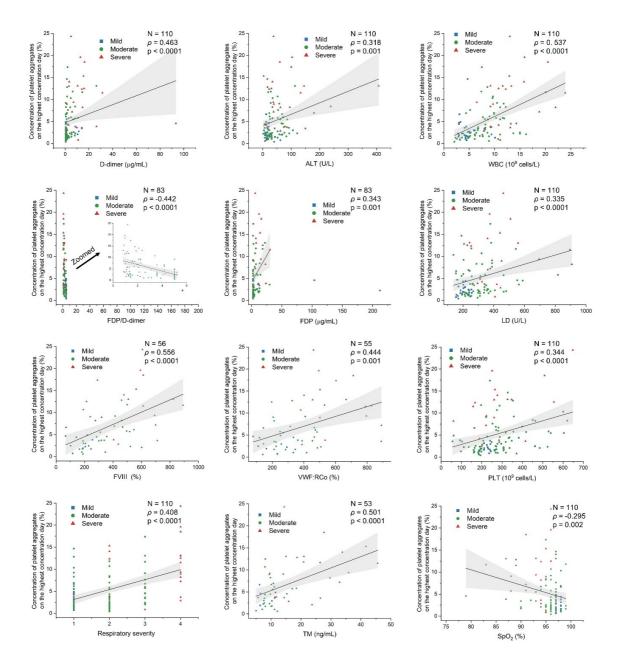
**Supplementary Fig. 1 | Detailed schematic of the FDM microscope.** CW: continuous wave; PBS: polarizing beamsplitter; HWP: half-wave plate; APD: avalanche photodetector; HPF: high-pass filter; DM: dichroic mirror; HBS: half beamsplitter; AOD: acousto-optic deflector; NA: numerical aperture. See "Optical frequency-division-multiplexed microscope" in the Methods section for details.



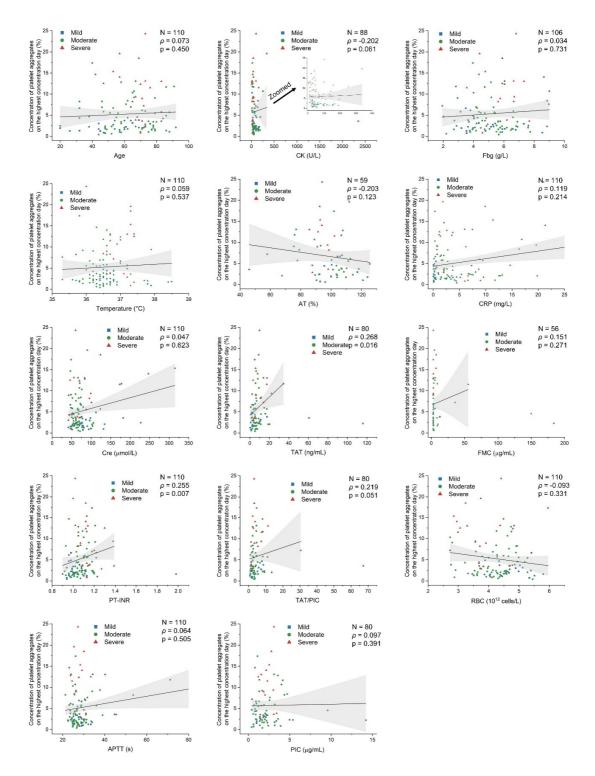
**Supplementary Fig. 2 | Images of single platelets and platelet aggregates. a,** Images of flowing single platelets and platelet aggregates obtained by the FDM microscope. **b,** Image of stationary single platelets, platelet aggregates, and leukocytes obtained by a conventional optical microscope. The sample was prepared using cytospin, followed by May-Giemsa staining. Both samples were obtained from a blood sample collected from a single COVID-19 patient on the same blood draw date.



**Supplementary Fig. 3 | Comparison with negative and positive control groups.** Negative control: healthy subjects (n = 67 biologically independent samples); positive control (n = 7 biologically independent samples): patients under no anticoagulant therapy with no abnormality confirmed by their coagulation tests (see "human subjects" in the Methods section for details); Mild: mild COVID-19 patients (n = 23 biologically independent samples); Moderate: moderate COVID-19 patients (n = 68 biologically independent samples); Severe: severe COVID-19 patients (n = 19 biologically independent samples). Samples were measured on the highest concentration day of each hospitalized patient. Exact p values were obtained using the Mann–Whitney U-test (two-sided) and shown in the figure. Source data are provided as a Source Data file.



Supplementary Fig. 4 | Strong correlations between the concentration of platelet aggregates and clinical laboratory and physical findings. Respiratory severity level 1: without oxygen administration; level 2: with oxygen administration of 0.5 - 4 L/min; level 3: with oxygen administration of  $\geq 5$  L/min; level 4: with tracheal intubation or VV-ECMO. Linear fits show the correlation between the concentration of platelet aggregates and each clinical parameter with a 95% confidence interval shown in gray calculated by the standard error of measured y values. P values were obtained using the two-sided ANOVA test and shown in the figure. Source data are provided as a Source Data file.

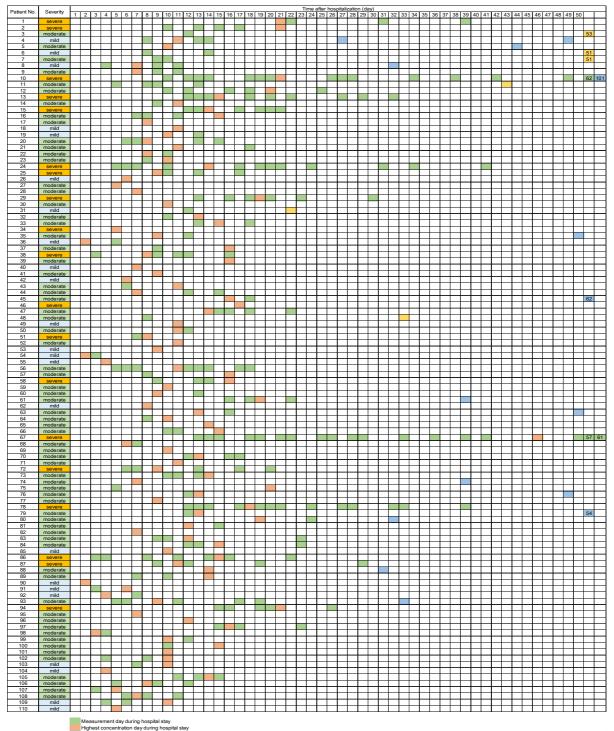


**Supplementary Fig. 5 | Weak correlations between the concentration of platelet aggregates and clinical laboratory and physical findings.** Linear fits show the correlation between the concentration of platelet aggregates and each clinical parameter with a 95% confidence interval shown in gray calculated by the standard error of measured y values. P values were obtained using the two-sided ANOVA test and shown in the figure. Source data are provided as a Source Data file.

Supplementary Data 1 | Demographics, clinical characteristics, and laboratory findings of patients with COVID-19. All the patients in this study were hospitalized at the University of Tokyo Hospital. Data are expressed as median values (IQR), n (%), or n/N (%). p values were calculated by the *t* test, Mann-Whitney U test, one-way ANOVA, chi-squared test, or Fisher's exact test.

Naio73 (6%)11 (4%)47 (6%)15 (7%)165 (6%)8 (7%)8 (7%)Female37 (2%)12 (5%)12 (5%)12 (5%)12 (5%)12 (5%)34 (4%)3 (2%)ConordellyIIIIIIIIIHypertension55 (5%)11 (4%)33 (4%)11 (5%)0.7544 (4%)6 (5%)0.93Dates35 (2%)7 (5%)19 (5%)9 (4%)0.7731 (3%)4 (4%)0.07Obsery, SM > 238 (5%)7 (5%)27 (4%)4 (1%)0.2236 (5%)2 (1%)0.04Coronary head filesses6 (5%)05 (5%)10 (5%)10 (5%)0.954 (4%)2 (1%)0.04Coronary head filesses9 (%)3 (1%)4 (6%)2 (1%)0.954 (4%)2 (1%)0.040.05Coronary head filesses9 (%)3 (1%)4 (6%)1 (6%)1 (6%)0.954 (4%)2 (1%)0.04Coronary head filesses9 (%)3 (1%)4 (6%)1 (6%)1 (6%)0.951 (6%)2 (1%)0.04Coronary head filesses9 (%)3 (1%)4 (6%)1 (6%)1 (6%)0.951 (6%)2 (1%)0.04Coronary head filesses9 (%)3 (1%)4 (6%)1 (6%)1 (6%)0.951 (6%)2 (1%)0 (1%)Coronary head filesses9 (%)3 (1%)4 (6%)1 (6%)1 (6%)0.951 (6%)1 (6%)1 (6%) <th></th> <th>All patients</th> <th>Mild patients</th> <th>Moderate patients</th> <th>Severe patients</th> <th>p value</th> <th>Survivors</th> <th>Non-survivors</th> <th>p value</th>		All patients	Mild patients	Moderate patients	Severe patients	p value	Survivors	Non-survivors	p value
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No.     No.     No.     No.     No.     No.     No.     No.     No.       Final     70 (%)     11 (%)     10 (%)     10 (%)     10 (%)     30 (%)     30 (%)       Final     70 (%)     11 (%)     20 (%)     10 (%)     30 (%) <t< td=""><td>Age, years</td><td>65.0 (52.0-73.5)</td><td>53.0 (36.0-65.0)</td><td>65.5 (53.3-78.0)</td><td>70.0 (65.0-73.0)</td><td>0.0004</td><td>62.0 (49.0-73.0)</td><td>83.0(72.0-88.0)</td><td>&lt; 0.0001</td></t<>	Age, years	65.0 (52.0-73.5)	53.0 (36.0-65.0)	65.5 (53.3-78.0)	70.0 (65.0-73.0)	0.0004	62.0 (49.0-73.0)	83.0(72.0-88.0)	< 0.0001
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Decision Decision Construction <br< td=""><td></td><td>55 (50%)</td><td>11 (48%)</td><td>33 (49%)</td><td>11 (58%)</td><td>0.75</td><td>49 (49%)</td><td>6 (55%)</td><td>0.95</td></br<>		55 (50%)	11 (48%)	33 (49%)	11 (58%)	0.75	49 (49%)	6 (55%)	0.95
Obleshy 681-2535 (95%)77 (95%)27 (4%)4 (1%)0 (2)36 (5%)2 (2%)2 (1%)0.04COPO4 (4%)03 (3%)4 (4%)1 (5%)0 (5%)2 (2%)2 (1%)0.052 (2%)2 (1%)0.05Chrone bard datasi5 (5%)05 (3%)4 (4%)2 (1%)0.054 (4%)2 (1%)0.051 (5%)2 (1%)0.050 (5%)2 (1%)0.050 (5%)2 (1%)0.050 (5%)2 (1%)0.050 (5%)2 (1%)0.050 (5%)0 (1%) <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>									
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Concomb Mart Glassa     Sp (S)     O     S (N)     I (R)     O (S)     4 (H)     2 (H)     0 (H)       Chronic floor diacaa     9 (R)     3 (13%)     4 (R)     2 (12%)     0.55     8 (R)     1 (P)     0 (P)       Chronic bloir diacaa     9 (R)     3 (13%)     4 (R)     2 (1%)     0.55     5 (R)     2 (18%)     0.14       Arbite malignamy     7 (R)     0     6 (R)     1 (R)     0.55     5 (R)     2 (18%)     0.14       Mitpoint diary about     7 (R)     3 (13%)     8 (R)     1 (R)     0.55     1 (R)     2 (R)     0.14       Mitpoint diary about     7 (R)     3 (17%)     8 (R)     1 (R)     0.55     0.55     0.55     0.55     0.55     0.55     0.55 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>									
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Add call count, ±10 <sup>3</sup> L     4.25 (3.80-462)     4.34 (3.72-499)     4.29 (3.94-463)     111 (3.99-36)     0.084     4.27 (3.88-46)     4.07 (3.44-46)     0.017       Platel count, ±10 <sup>3</sup> L     225 (181-8293)     227 0 (175-02450)     246 (183-102)     210 (190-02820)     0.032     230 (166-0306)     180 (132-2090)     0.017       AT, UL     27.5 (14.0-48)     130 (12.0-27.0)     310 (17.0-51.3)     30 (14.0-105.)     0.013     250 (14.0-49.0)     50.0 (75.0-22.0)     0.023       Creatine shydrogenase, UL     301 (22.0-37.9)     2050 (160-024.0)     305 (238-339.0)     600.084.0-660.0)     <0.001     6.37 (30-20.5)     38.1 (25.75.9)     0.0077       PfAiR     1.05 (1.00-113)     0.90 (98-103)     1.07 (1.02-113)     1.31 (1.07-122)     0.36     105 (1.00-113)     106 (98-122)     0.47       APTT, s     27.6 (25.43.09)     28.8 (25.1-20.0)     27.2 (25.1-38.0)     0.0075     27.2 (25.1-29.8)     38.4 (23.2-45.5)     <0.0071       S1     4.46 (44.5)     1.9 (35.5)     2.7 (15.2-13.0)     2.8 (17.5 75.9)     0.0011     4.7 (17.5)     0.6 (98-122)     0.0071       Defamer, japint	measurement day	64(4208)	40/3148)	69/4796)	11 1 (0 0 14 5)	< 0.0001	61(1207)	8 / (7 0 10 7)	0.13
Paralest count, *10 <sup>7</sup> /L     285 (818-293)     270 (750-2450)     245 (880-332.0)     0.02     243.0 (86.0-386.0)     180.0 (13.0-20.0)     0.017       A.T. UL     27.5 (14.048.8)     13.0 (12.0-27.0)     31.0 (70.51.3)     34.0 (14.0460.0)     0.013     25.0 (14.049.0)     55.0 (77.042.0)     0.23       Creatinine, µmolL     68.4 (58.190.7)     64.5 (48.74.77)     68.4 (60.81.80     68.6 (92.116.8)     0.42     68.1 (57.57.96)     70.0 (90.043.00)     64.0 (42.0-68.0)     <0.0017       Creatine phydrogenase, UL     91.0 (22.08.379.5)     0.20 (09.25.2)     52.4 (2.09.44)     66.6 (7.2-18.8)     <0.0001     63.7 (30.20.25)     38.8 (2.57.50)     0.0077       Creative protein, mglL     41.5 (1.547.87)     0.32 (0.92.52)     52.4 (2.09.44)     66.6 (7.2-18.8)     0.00075     27.2 (25.12.8)     38.4 (23.45.5)     <0.0071       Creative protein, mglL     415 (1547.87)     0.32 (0.92.52)     52.4 (2.09.44)     66.6 (7.2-18.8)     0.00075     27.2 (25.12.8)     38.4 (23.45.5)     <0.0071       Creative protein, mglL     48 (4%%)     19 (85%)     27.4 (25.13.0)     13.8 (22.41.0)     16.8 (60.00.13)     10.0 (13.0.20.07)									
AT, UL     27.5 (14.049.8)     13.0 (12.027.0)     31.0 (17.051.3)     34.0 (14.016.0)     0.013     25.0 (14.049.0)     35.0 (17.042.0)     0.23       Creatinine, µmolL     69.4 (58.140.7)     64.5 (54.8-78.7)     69.4 (61.041.8)     68.8 (50.211.6)     0.42     68.1 (57.573.6)     76.0 (60.0156.6)     0.25       Creatine phylorgenae, UL     31.0 (12.08.375.9)     205.0 (169.0-240.0)     51.0 (22.03.336.0)     50.0 (28.4 (20.40.0)     6.6 (3.721.81)     < 0.0001     6.37 (0.22.05.6)     88.8 (125.75.0)     0.0077       Pri-NR     10.6 (1.00-11.3)     0.9 (9.86-1.03)     107 (1.02-11.3)     113 (1.07-122)     0.36     1.05 (1.00-1.3)     106 (0.88-1.22)     0.46       APTT, a     27.6 (25.43.09)     28.8 (25.12.00)     27.2 (25.13.07)     29.5 (74.36.0)     0.0075     27.2 (51.28.8)     88.4 (23.45.5)     <0.0001       O-dimer, µg/mL     1     48.6 (4%.)     19.(3%.)     28.6 (1.40.9)     1.05 (1.00-1.3)     1.09 (1.00.100.000       C 1     6.2 (55%.)     1.19 (3%.)     2.8 (41.05.)     1.6 (5%.)     0.0071     3.0 (20.23.000.000.000.0000     3.0 (77.7%.)     8.7 (7%.)     8.7 (7%.) <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>									
Creatinine, µmo/L     69.4 (68.1-80.7)     64.5 (64.8-78.7)     69.4 (61.0-81.8)     69.8 (60.2-115.8)     0.42     68.1 (57.57.9)     76.0 (69.0-155.6)     0.25       Lactate dehydrogenese, UL     301.0 (220.8-379.5)     205.0 (168.0-240.0)     310.5 (238.3-358.0)     560.0 (840.0660.0)     < 0.0001									
Lactate delydrogenase, UL     301.0 (220.8-379.5)     205.0 (168.0-240.0)     310.5 (238.3-359.0)     560.0 (840.6660.0)     < 0.0001     657.0 (320.0560.0)     664.0 (342.0-636.0)     < 0.0007       C-auscive protein, mgL     4.15 (1.547.87)     0.32 (0.09-252)     5.24 (2.20-9.44)     6.66 (3.72-18.81)     < 0.0001     6.37 (3.02-20.56)     3.88 (1.25-7.50)     0.0077       PT-NR     1.05 (1.00-1.13)     0.99 (0.88-1.03)     1.07 (1.02-1.13)     1.13 (107-1.22)     0.36     1.05 (1.00-1.13)     1.66 (0.98-1.22)     0.46       APTT, s     27.6 (25.4-30.9)     26.8 (25.1-28.0)     27.2 (25.1-30.7)     29.5 (27.4-36.0)     0.00075     27.2 (25.1-29.8)     3.84 (32.345.5)     <0.0001       D-dimer, µg/mL     -     -     -     -     -     -     -     -     -       S-1     62 (65%)     4 (17%)     40 (69%)     18 (65%)     0.074     76 (77%)     8 (73%)     0.72       S-1     62 (65%)     4 (23,724.98)     4.36 (3.94-4.68)     371 (3.05-4.38)     0.0007     4.36 (3.824.70)     3.64 (2.94.28)     0.0014       D-1000000000000000000000000000000000000				. ,					
Creactive protein, mg/L     4.15 (1.54-7.87)     0.32 (0.09-2.52)     5.24 (2.09.44)     6.66 (3.72-18.81)     < 0.0001     6.37 (3.02-0.56)     3.88 (1.25-7.50)     0.0077       PT-NR     1.05 (1.00-1.13)     0.99 (9.98-1.03)     1.07 (1.02-1.13)     1.13 (1.07-1.22)     0.36     1.06 (1.00-1.13)     1.06 (0.98-1.22)     0.46       APTT, s     27.6 (55-30.9)     26.8 (25-1.29.0)     27.2 (25.1-30.7)     29.5 (27.4-36.0)     0.0075     27.2 (25.1-29.8)     3.84 (92.3-45.5)     <.0001       D-dimer, µg/mL     T     T     T     T     T     T     T     T     T       ≤ 1     44 (4%)     19 (3%)     28 (4%)     1 (5%)     <.0001     47 (47%)     1 (9%)     0.022       > 1     65 (56%)     4 (17%)     40 (95%)     18 (95%)     0.074     76 (7%)     8 (73%)     0.72       abordroty findings on the platest consentration day     44 (3 (3.2-50)     8.2 (5.4-10.5)     12 9 (9.7-159)     < 0.001     7.6 (4.5-10.1)     13.3 (8.2-0.1)     < 0.0001       Red cell count, x10 <sup>7</sup> /L     4.29 (3.72-468)     4.42 (3.2-2.09)     3.6 (3.894-68)									
PT-NR     1.05 (1.00-1.13)     0.99 (0.98-1.03)     1.07 (1.02-1.13)     1.13 (1.07-1.22)     0.36     1.05 (1.00-1.13)     1.06 (0.98-1.22)     0.46       APTT, s     27.6 (25.4-30.9)     28.8 (25.1-29.0)     27.2 (25.1-30.7)     29.5 (27.4-36.0)     0.0075     27.2 (25.1-29.8)     38.4 (32.3-45.5)     < 0.0001       D-dimer, µg/mL <th< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>									
APTT, s     27.6 (25.4-30.9)     26.8 (25.1-29.0)     27.2 (25.1-30.7)     29.5 (27.4-36.0)     0.0075     27.2 (25.1-29.8)     38.4 (32.3-45.5)     < 0.0001       L-dimer, µg/mL     Image:									
D-dimer, µg/ml.     Image: Participant of the participant of the participant of the participant of the participant definition of participant definition definite definition definited efinition definited efinition def									
≤1     48 (44%)     19 (83%)     28 (41%)     1 (5%)     < 0.0001     47 (47%)     1 (9%)     0.022       >1     62 (56%)     4 (17%)     40 (59%)     18 (95%)     0.074     52 (53%)     10 (91%)     0.022       Anticoagulant therapy on the lighest concentration day abcrotropt findings on the lighest concentration day     84 (76%)     15 (65%)     51 (75%)     18 (95%)     0.074     76 (77%)     8 (73%)     0.72       abcrotropt findings on the lighest concentration day     84 (76%)     4.3 (3.2-5.0)     8.2 (5.410.5)     12.9 (9.7-15.9)     <0.001     76 (4.5-10.1)     13.3 (8.2-20.1)     <0.0001       Red cell count, ×10 <sup>7</sup> /L     4.29 (3.72-4.68)     4.42 (3.72-4.99)     4.36 (3.84-68)     3.71 (3.06-4.38)     0.0027     4.36 (3.82-4.70)     3.64 (2.994.28)     0.0046       Platelet count, ×10 <sup>7</sup> /L     263.0 (197.8327.3)     27.0 (185.0-245.0)     27.6 (0.20-337.0)     26.10 (202.0-371.0)     0.046     269.0 (200.032.0)     28.0 (28.0-28.0)     0.019       ALT, U/L     31.0 (16.0-62.0)     16.0 (12.0-25.0)     33.5 (19.3-68.0)     36.0 (22.0-37.0)     0.017     30.0 (15.6-62.0)     36.0 (28.0-26.0)		27.6 (25.4-30.9)	26.8 (25.1-29.0)	27.2 (25.1-30.7)	29.5 (27.4-36.0)	0.0075	27.2 (25.1-29.8)	38.4 (32.3-45.5)	< 0.0001
>1     62 (56%)     4 (17%)     40 (59%)     18 (95%)     52 (53%)     10 (91%)       Anticoagulant therapy on the highest concentration day aboratory findings on the highest concentration day     84 (76%)     15 (65%)     51 (75%)     18 (95%)     0.074     76 (77%)     8 (73%)     0.72       aboratory findings on the highest concentration day     8.3 (04.7-10.9)     4.3 (3.2-5.0)     8.2 (5.4-10.5)     12.9 (9.7-15.9)     <0.0001									
Anticoagulant therapy on the tighest concentration day aboratory findings on the tighest concentration day thest concentration day     84 (76%)     15 (65%)     51 (75%)     18 (95%)     0.074     76 (77%)     8 (73%)     0.72       aboratory findings on the tighest concentration day     8.0 (4.7-10.9)     4.3 (3.2-5.0)     8.2 (5.4-10.5)     12.9 (9.7-15.9)     <0.0001						< 0.0001			0.022
highest concentration day chocatory findings on the injeast concentration day chocatory findings on the injeast concentration day check column, ×10 <sup>17</sup> L     64 (0%)     15 (05%)     51 (0%)     18 (95%)     0.014     76 (7%)     8 (3%)     0.72       Laboratory findings on the injeast concentration day Laboratory findings on the injeast concentration day     8.0 (4.710.9)     4.3 (3.25.0)     8.2 (5.410.5)     12.9 (9.715.9)     <0.001									
Red cell count, x10 <sup>37</sup> L     4.29 (3.724.68)     4.42 (3.724.99)     4.36 (3.84.68)     3.71 (3.064.38)     0.0027     4.36 (3.824.70)     3.64 (2.994.28)     0.0046       Platelet count, x10 <sup>37</sup> L     4.29 (3.724.68)     4.42 (3.724.99)     4.36 (3.84.68)     3.71 (3.064.38)     0.0027     4.36 (3.824.70)     3.64 (2.994.28)     0.0046       Platelet count, x10 <sup>37</sup> L     263.0 (197.8327.3)     227.0 (165.0-245.0)     27.60 (202.0-337.0)     261.0 (202.0-371.0)     0.046     269.0 (200.0-332.0)     221.0 (158.0-261.0)     0.019       ALT, U/L     31.0 (16.0-62.0)     16.0 (12.0-25.0)     33.5 (193.48.8)     38.0 (22.0-78.0)     0.017     30.0 (15.0-62.0)     38.0 (28.0-92.0)     0.19       Creatinine, µmol/L     68.5 (65.7-83.3)     69.0 (54.8-70.7)     68.1 (57.7-91.1)     69.8 (54.8-100.8)     0.32     67.2 (54.8-77.8)     100.8 (83.1-173.3)     0.12       Lactale dehydrogenase, U/L     280.0 (215.8-374.0)     210.0 (170.0-240.0)     301.0 (229.8-363.3)     420.0 (324.0-509.0)     <0.0001     257.0 (211.0-351.0)     544.0 (389.0-695.0)     <0.0001       C-reactive protein, mg/L     252 (0.63-6.96)     0.39 (0.99-2.67)     2.72 (1.05-7.7)     60.1 (1	highest concentration day Laboratory findings on the highest concentration day	84 (76%)	15 (65%)	51 (75%)	18 (95%)	0.074	76 (77%)	8 (73%)	0.72
Platelet count, ×10 <sup>3</sup> /L     263.0 (197.8-327.3)     27.0 (185.0-245.0)     276.0 (202.0-337.0)     261.0 (202.0-371.0)     0.046     269.0 (200.0-332.0)     221.0 (158.0-261.0)     0.019       AT, U/L     31.0 (16.0-62.0)     16.0 (12.0-25.0)     33.5 (19.3-68.0)     38.0 (22.0-78.0)     0.017     30.0 (15.0-62.0)     38.0 (28.0-92.0)     0.19       Creatinine, µmol/L     68.5 (55.7-83.3)     69.0 (54.8-78.7)     68.1 (57.7-79.1)     69.8 (54.810.0)     0.32     67.2 (54.8-77.0)     100.8 (83.1-173.3)     0.12       Lactate dehydrogenase, U/L     20.0 (215.8-37.40)     0.30 (10.0-240.0)     30.1 (228.8-36.3)     20.0 (324.0-509.0)     < 0.0001     25.7 0.211.0-351.0)     54.40 (389.0-689.0)     < 0.0001       C-reactive protein, mg/L     2.52 (0.63-6.90)     0.39 (0.92-257)     2.72 (1.05-7.27)     6.01 (18.3196.2)     0.0001     2.23 (0.51-6.60)     9.45 (1.11-6.31)     < 0.0001       PT-NR     10.8 (1.01-1.13)     0.99 (0.88-1.60)     1.09 (1.03-1.15)     1.12 (1.05-1.16)     0.0059     1.06 (1.00-1.13)     1.14 (1.08-1.20)     0.0107       APT, s     27.2 (25-2.30.1)     2.68 (25.1-2.90)     2.68 (25.2-3.04)     2.88 (26.2-33.4) <th< td=""><td>Leukocyte count, ×10<sup>9</sup>/L</td><td>8.0 (4.7-10.9)</td><td>4.3 (3.2-5.0)</td><td>8.2 (5.4-10.5)</td><td>12.9 (9.7-15.9)</td><td>&lt; 0.0001</td><td>7.6 (4.5-10.1)</td><td>13.3 (8.2-20.1)</td><td>&lt; 0.0001</td></th<>	Leukocyte count, ×10 <sup>9</sup> /L	8.0 (4.7-10.9)	4.3 (3.2-5.0)	8.2 (5.4-10.5)	12.9 (9.7-15.9)	< 0.0001	7.6 (4.5-10.1)	13.3 (8.2-20.1)	< 0.0001
ALT, U/L     31.0 (16.0÷2.0)     16.0 (12.0±5.0)     33.5 (19.3+68.8)     38.0 (22.0+78.0)     0.017     30.0 (15.0÷2.0)     38.0 (28.0+20.0)     0.19       Creatinine, µm0/L     68.5 (55.78.3.3)     69.0 (54.8-77.7)     68.1 (57.7+7.9)     69.8 (64.8+10.8)     0.32     67.2 (54.8-77.8)     100.8 (83.1173.3)     0.12       Lactate dehydrogenase, U/L     280.0 (215.8-37.40)     210.0 (170.0-240.0)     30.1 (228.363.3)     420.0 (324.0-590.0)     <0.0001	Red cell count, ×10 <sup>12</sup> /L	4.29 (3.72-4.68)	4.42 (3.72-4.99)	4.36 (3.98-4.68)	3.71 (3.06-4.38)	0.0027	4.36 (3.82-4.70)	3.64 (2.99-4.28)	0.0046
Creatinine, µmol/L     68.5 (55.7.83.3)     69.0 (54.8.78.7)     68.1 (57.7.91.1)     69.8 (54.8100.8)     0.32     67.2 (54.8.77.8)     100.8 (83.1-173.3)     0.12       Lactate dehydrogenase, UL     200.0 (216.8-374.0)     210.0 (170.0-240.0)     30.10 (229.8-363.3)     420.0 (324.0-509.0)     < 0.0001     257.0 (211.0-351.0)     64.0 (389.0-695.0)     < 0.0001       C-reactive protein, mg/L     2.52 (0.63.6.96)     0.39 (0.09.2.57)     2.72 (1.05.7.27)     6.01 (1.83·19.62)     0.0004     2.23 (0.51.660)     9.45 (1.11-26.31)     < 0.0001       PT-NR     1.08 (1.01-1.13)     0.99 (0.98-1.06)     1.09 (1.03-1.15)     1.12 (1.05-1.16)     0.0059     1.06 (1.00-1.13)     1.14 (1.08-1.20)     0.017       APTT, s     27.2 (2.52-30.1)     26.8 (2.51-29.0)     26.8 (2.50-30.1)     28.8 (2.62-33.4)     0.44     26.8 (2.51-29.0)     37.8 (3.0.55.6)     < 0.0001       D-dimer, µg/mL	Platelet count, ×10 <sup>9</sup> /L	263.0 (197.8-327.3)	227.0 (185.0-245.0)	276.0 (202.0-337.0)	261.0 (202.0-371.0)	0.046	269.0 (200.0-332.0)	221.0 (158.0-261.0)	0.019
Lactate dehydrogenase, UL     280.0 (215.8-37.4)     210.0 (170.0-240.0)     301.0 (229.8-363.3)     420.0 (324.0-509.0)     < 0.0001     257.0 (211.0-51.0)     544.0 (389.0695.0)     < 0.0001       C-reactive protein, mg/L     2.52 (0.63.6-96)     0.39 (0.09-2.57)     2.72 (1.05-7.27)     6.01 (1.83.19.62)     0.0004     2.23 (0.51.660)     9.45 (1.11-26.31)     < 0.0001       PT-NR     1.08 (1.01-1.13)     0.99 (0.98-1.06)     1.09 (1.03-1.15)     1.12 (1.05-1.16)     0.0059     1.06 (1.00-1.13)     1.14 (1.08-1.20)     0.017       APTT, s     27.2 (2.52.30.1)     26.8 (25.1-29.0)     26.8 (25.0-30.1)     28.8 (26.2-33.4)     0.44     26.8 (25.1-29.0)     37.8 (30.5-5.6)     < 0.0001       D-dimer, µg/mL	ALT, U/L	31.0 (16.0-62.0)	16.0 (12.0-25.0)	33.5 (19.3-68.8)	38.0 (22.0-78.0)	0.017	30.0 (15.0-62.0)	38.0 (28.0-92.0)	0.19
C-reactive protein, mg/L     2.52 (0.63.6.99)     0.39 (0.09-2.67)     2.72 (1.05-7.27)     6.01 (1.83.19.62)     0.0004     2.23 (0.51.6.60)     9.45 (1.11-26.31)     < 0.0001       PT-NR     1.08 (1.01-1.13)     0.99 (0.98-1.66)     1.09 (1.03-1.15)     1.12 (1.05-1.16)     0.0059     1.06 (1.00-1.13)     1.14 (1.08-1.20)     0.017       APT. s     27.2 (25-30.1)     26.8 (25.1-29.0)     26.8 (26.2-33.4)     0.44     26.8 (25.1-29.0)     37.8 (30.553.6)     <0.0001       D-dimer, µg/mL     43 (39%)     19 (83%)     23 (34%)     1 (5%)     <0.0001     43 (43%)     0.0     0.0002	Creatinine, µmol/L	68.5 (55.7-83.3)	69.0 (54.8-78.7)	68.1 (57.7-79.1)	69.8 (54.8-100.8)	0.32	67.2 (54.8-77.8)	100.8 (83.1-173.3)	0.12
PT-NR     1.08 (1.01-1.13)     0.99 (0.98-1.06)     1.09 (1.03-1.15)     1.12 (1.05-1.16)     0.0059     1.06 (1.00-1.13)     1.14 (1.08-1.20)     0.017       APT, s     27.2 (25-23.01)     26.8 (25.1-29.00)     26.8 (25.0-30.1)     28.8 (26.2-33.4)     0.44     26.8 (25.1-29.00)     37.8 (30.5-53.6)     <0.0001	Lactate dehydrogenase, U/L	280.0 (215.8-374.0)	210.0 (170.0-240.0)	301.0 (229.8-363.3)	420.0 (324.0-509.0)	< 0.0001	257.0 (211.0-351.0)	544.0 (389.0-695.0)	< 0.0001
APTT, s     27.2 (25.2·30.1)     26.8 (25.1·29.0)     26.8 (25.0·30.1)     28.8 (26.2·33.4)     0.44     26.8 (25.1·29.0)     37.8 (30.5·53.6)     <0.0001       D-dimer, µg/mL     43 (39%)     19 (83%)     23 (34%)     1 (5%)     <0.0001     43 (43%)     0     0.0002	C-reactive protein, mg/L	2.52 (0.63-6.96)	0.39 (0.09-2.57)	2.72 (1.05-7.27)	6.01 (1.83-19.62)	0.0004	2.23 (0.51-6.60)	9.45 (1.11-26.31)	< 0.0001
D-dimer, μg/mL ≤1 43 (39%) 19 (83%) 23 (34%) 1 (5%) <0.0001 43 (43%) 0 0.0002	PT-INR	1.08 (1.01-1.13)	0.99 (0.98-1.06)	1.09 (1.03-1.15)	1.12 (1.05-1.16)	0.0059	1.06 (1.00-1.13)	1.14 (1.08-1.20)	0.017
≤1     43 (39%)     19 (83%)     23 (34%)     1 (5%)     <0.0001     43 (43%)     0     0.0002	APTT, s	27.2 (25.2-30.1)	26.8 (25.1-29.0)	26.8 (25.0-30.1)	28.8 (26.2-33.4)	0.44	26.8 (25.1-29.0)	37.8 (30.5-53.6)	< 0.0001
	D-dimer, µg/mL								
>1     67 (61%)     4 (17%)     45 (66%)     18 (95%)     56 (57%)     11 (100%)	≤1	43 (39%)	19 (83%)	23 (34%)	1 (5%)	< 0.0001	43 (43%)	0	0.0002
	>1	67 (61%)	4 (17%)	45 (66%)	18 (95%)		56 (57%)	11 (100%)	

Supplementary Data 2 | Measurement days of patients with COVID-19. Most patients were tested during their hospital stays while some patients were tested at the time of outpatient consultations after their discharge from the hospital.



Highest concentration day during hospital stay Outpatient consultation day after discharge from hospital Highest concentration day after discharge from hospital **Supplementary Data 3 | Additional laboratory findings of patients with COVID-19.** All the patients in this study were hospitalized at the University of Tokyo Hospital. p values were calculated by *t* test, Mann-Whitney U test, one-way ANOVA, chi-squared test, or Fisher's exact test.

	All patients	Mild patients	Moderate patients	Severe patients	p value	Survivors	Non-survivors	p value
FVIII, %	329.2 (205.7-514.9) n = 56	189.8 (102.8-220.1) n = 11	342.4 (219.9-497.2) n = 30	563.1 (404.9-612.4) n = 15	< 0.0001	311.0 (191.1-464.7) n = 45	517.3 (301.1-692.7) n = 11	0.0013
TM, ng/mL	11.2 (8.1-18.6) n = 53	7.7 (6.4-10.6) n = 10	10.8 (8.8-16.2) n = 29	24.4 (11.7-34.3) n = 14	< 0.0001	10.2 (8.0-12.7) n = 42	26.4 (20.9-32.9) n = 11	< 0.0001
VWF:Rco, %	380.9 (224.1-494.5) n = 55	232.1 (120.2-292.9) n = 11	380.9 (224.1-483.5) n = 31	501.4 (427.9-751.2) n = 13	0.0001	333.5 (218.0-463.7) n = 45	660.6 (476.3-843.4) n = 10	< 0.0001
FDP, µg/mL	3.4 ( 2.5-10.9) n = 83	2.5 (2.5-3.5) n = 16	3.4 (2.5-9.2) n = 52	12.3 (5.9-18.6) n = 15	0.50	3.4 (2.5-8.3) n = 72	13.2 (7.1-22.9) n = 11	0.28
TAT, ng/mL	6.0 (3.5-10.2) n = 80	3.1 (1.5-7.9) n = 16	6.3 (4.3-10.4) n = 50	8.6 (5.3-14.8) n = 14	0.35	5.5 (3.1-8.9) n = 69	17.5 (10.8-22.1) n = 11	0.0031
FMC, µg/mL	3.0 (3.0-5.4) n = 55	3.0 (3.0-3.2) n = 11	3.0 (3.0-4.0) n = 31	4.8 (3.0-10.2) n = 13	0.70	3.0 (3.0-3.8) n = 45	6.1 (3.0-16.5) n = 10	0.20
PIC, µg/mL	1.9 (1.1-3.0) n = 80	1.0 (0.8-2.0) n = 16	1.9 (1.3-3.2) n = 50	2.2 (1.7-3.0) n = 14	0.16	1.9 (1.1-3.1) n = 69	1.6 (1.3-2.3) n = 11	0.25
Fbg, g/L	5.17 (4.03-6.20) n = 106	4.12 (3.55-5.55) n = 22	5.32 (4.19-6.33) n = 65	5.90 (4.59-6.69) n = 19	0.085	5.18 (4.17-6.20) n = 95	4.74 (2.95-5.63) n = 11	0.085
AT, %	100.0 (90.9-107.1) n = 59	100.4 (92.8-117.3) n = 11	103.5 (88.3-107.5) n = 33	93.9 (90.9-98.6) n = 15	0.19	101.6 (92.6-108.3) n = 48	77.8 (67.7-98.6) n = 11	< 0.0001
CK, U/L	47.0 ( 28.0-97.0) n = 87	56.5 (35.5-87.8) n = 16	50.0 (28.5-104.0) n = 53	38.0 (24.0-97.8) n = 18	0.72	47.0 (28.0-98.0) n = 77	46.5 (32.0-112.5) n = 10	0.0044

**Supplementary Data 4 | Multivariate regression analysis.** The upper part shows the first analysis while the lower part shows the second analysis, to determine explanatory factors for predicting the concentration of platelet aggregates on the highest concentration day.

Objective factor Explanatory factor			Concentration of platelet aggregates on the highest concentration day		
		Standardized coefficient (β)	p value		
	FVIII	0.568	< 0.001		
Vascular endothelial	тм		NS		
disorder markers	VWF:Rco		NS		
	R <sup>2</sup>	0.322 (p < 0	0.001)		
	PT-INR	0.222	0.049		
	D-dimer		NS		
Coagulation / fibrinolysis markers	FDP		NS		
	TAT		NS		
	R <sup>2</sup>	0.049 (p = 0.049)			
	WBC	0.265	0.009		
	Respiratory severity	0.306	0.002		
	PLT	0.227	0.006		
	LD		NS		
Other markers	ALT		NS		
	SpO <sub>2</sub>		NS		
	Survival		NS		
	Gender		NS		
	R <sup>2</sup>	0.364 (p < 0	0.001)		

Obje	ctive factor	Concentration of platelet aggregates on the highest concentration day		
Explanatory factor		Standardized coefficient (β)	p value	
Selected markers	Respiratory severity	0.355	0.009	
	FVIII	0.323	0.016	
	WBC		NS	
	PLT		NS	
	PT-INR		NS	
	R <sup>2</sup>	0.352 (p	< 0.001)	

Supplementary Data 5 | Demographics, clinical characteristics, and laboratory findings of patients with other diseases. All the patients in this study were hospitalized at the University of Tokyo Hospital. Data are expressed as median values (IQR) or n/N (%).

	Positive control
	n = 7
Age, years	47.0 (17.0-70.0)
Sex	
Male	3 (43%)
Female	4 (57%)
Comorbidity	
Hypertension	2 (29%)
Diabetes	1 (14%)
Obesity, BMI > 25	1 (14%)
Coronary heart disease	0
Active malignancy	0
Antiplatelet therapy	0
Anticoagulant therapy	0
Laboratory findings	
Leukocyte count, ×109/L	5.1 (4.7-5.2)
Platelet count, ×109/L	238.0 (218.5-283.0)
ALT, U/L	19.0 (15.5-29.0)
Creatinine, μmol/L	64.5 (59.7-74.7)
Lactate dehydrogenase, U/L	216.0 (196.0-223.0)
C-reactive protein, mg/L	0.02 (0.02-0.05)
D-dimer, μg/mL	0.5 (0.5-0.7)