SUPPLEMENTAL MATERIAL

Data Disclosure Statement
All data, analytic methods and study materials supporting the findings of this study are provided in the manuscript and supplemental material and are available from the corresponding author upon reasonable request.

EXPERIMENTAL MODEL AND SUBJECT DETAILS
Consecutive patients with confirmed COVID-19 (total of 115 patients) including severe and non-severe forms were admitted at Cheikh Zaïd Hospital from March 06, 2020 to May 20, 2020. The male/female ratio was 1.3:1. The mean age of patients was 52.44 ± 20.15 with 54 ± 20.48 and 51 ±19.92 for female and male respectively. Control group for plasma analysis assays and experiments on platelets lysates and aggregation was selected to be sex and age matched with COVID-19 patients with a male/female ratio of 1.24:1 and a mean age of 50.15 ± 17.98. Patients with negative RT-PCR findings for SARS-CoV-2 did not serve as healthy controls in the study, as these patients were still sick and presented with similar symptoms as COVID-19 but of unknown etiology.

The overall study design was not blinded as patients were initially classified by symptoms, presence of viral RNA and disease severity. These parameters were known when blood was collected by the clinicians. However, the analyses were blinded in the following assays: Measurements of cytokine profiles, Extracellular-Vesicle measurements, PF4 and Serotonin measurements.

Ethics Statement
This study was approved by the Local Ethics Committee of Cheikh Zaid Hospital, Rabat, Morocco and complies with the Declaration of Helsinki.

Patient inclusion criteria
Individuals suspected of SARS-CoV-2 infection (travelers, proximity to infected patients and presence of symptoms) were recruited with informed consent at Cheikh Zaïd Hospital in Rabat, Morocco. Patients were diagnosed as COVID-19-positive by nucleic acid test and were classified as non-severe or severe in accordance with the clinical classification of the degree of severity of COVID-19. Patients were tested for COVID-19-positivity at 5 time-points: On Admission (Day 0), Day 6, Day 13, Day 20, Day 30+.

Patient exclusion criteria for platelet functional assays
Patients with chronic diseases and those who took medications that interfere with platelet function within 2 weeks prior to experimentation were excluded from the study. Chronic Diseases: Hypertension, Diabetes, Cancer, Heart Diseases. Medications: Aspirin, Prasugrel, Clopidogrel, Ticagrelor, Cangrelor, Cilostazol, Dipyridamole, Abciximab, Eptifibatide, Tirofiban, Non-steroidal anti-inflammatory drugs (NSAIDs)

METHOD DETAILS
Clinical data and blood work
All laboratory blood work was performed in the COVID-19 laboratory dedicated to the pandemic only at Cheikh Zaïd Hospital. Patients’ demographic data, clinical reports,
laboratory blood work results, and treatment protocols were collected, analyzed and compared for clinical outcomes.

**Lung computed tomography**
Lung infection by COVID-19 was assessed by high-resolution computed tomography, using a multi slice helical CT without intravenous contrast (Siemens, Straton MX P; Erlangen, Germany).

**Detection of SARS-CoV-2 using one-step RT-PCR**
Total RNA was extracted from exfoliated cells from the nasal cavity using MagPurix Extraction system. A one-step real-time PCR kit (Tib-Molbiol, Berlin) for the detection of 2019-nCoV RdRp and E genes was purchased from Qiagen. The PCR reactions were performed using the Rotor-Gene Q thermocycler (Hilden, Germany). The PCR program consisted of 50°C for 15 min, 95°C for 5 min, 45 cycles of 95°C for 10 sec, 55°C for 45 sec, and was terminated by dissociation. Synthetic RNA for 2019-nCoV E gene and RdRp assay were used as positive controls (ACAGGTACGTTAATAGTTAATAGCGT and GTGARATGGTCAATGTGTGGCGG for E and RdRp genes respectively). For the detection of SARS-CoV-2 RNA in platelets, platelet rich plasma PRP filtration and magnetic bead-mediated leukocyte and erythrocyte depletion were performed. From each platelet concentrate with total platelet numbers in the range of 2.2–2.8 × 10^{11} (mean, 2.5 × 10^{11}) we obtained 20.4–26.8 μg (mean, 23.2 μg) of total RNA. The total elution volume from the MagPurix Extraction system was 50 μL.

**ACE2 detection by qRT-PCR**
ACE2 mRNA was evaluated in platelets using an intron-spanning set of primers previously described\textsuperscript{74} and the SsoAdvanced Universal SYBR Green Supermix (BioRad, CA, USA). HACE2 (NM_021804) primer sequences: Forward, 5' AAACATACTGTGACCCCGCAT 3' and Reverse 5' CCAAGCCTCAGCATATTGAACA 3'. A one step real time PCR program was assessed: 3 min at 96°C followed by 45 cycles at 95°C for 10 sec, 60°C 25 sec. A Rotor-Gene Q thermocycler was used (Hilden, Germany). Further analysis (Online Figure IX B and D): Non-intron spanning primers: human ACE2 PrimePCR Probe Assay (BioRad, CA, USA) and PrimePCR DNA Contamination Control Probe Assay, Human (BioRad, CA, USA).

**Assessment of cytokines and products of platelet degranulation in plasma and in platelet lysates**
Cytokine levels in plasma and platelets were assessed by Eve Technologies Corp. (Calgary, AB, Canada) using the Human Cytokine Array / Chemokine Array 48-Plex (HD48). If cytokines were not detected, a concentration corresponding to the lowest value extrapolated from the standard curve was attributed to the sample for quantification and comparison analyses. PF4 contained in plasma or platelet lysate was measured using the human CXCL4/PF4 DuoSet ELISA (R&D systems, MN, USA) according to the manufacturer’s protocol. Samples were diluted to fall within the detection range of the ELISA kit. The Serotonin ELISA Fast Track kit (LDN, Nordhorn, Germany) was used to determine serotonin concentration in plasma and platelet lysates, according to the manufacturer’s instructions.
Quantification of extracellular vesicles in patient plasma
Platelet rich plasma was centrifuged at 1000 g for 10 min to obtain plasma for EV-analysis. Platelet extracellular vesicles (EV) were measured by flow cytometry using a FACS Canto-II combined with a forward scatter (FSC) coupled to a photomultiplier tube (PMT) "small particles option" flow cytometer (BD Biosciences, CA, USA). The EV gate was generated using fluorescent silica beads of 0.1 µm, 0.5 µm and 1 µm (Kisker Biotech, Germany). EV were quantified using 2 µm fluorescent beads of known concentration (Silica particles, #si1u-S5-1, Nanocs Inc., NY, USA). EV in plasma were labeled for 30 min at room temperature with anti-human CD41 antibody conjugated to FITC (clone HIP8, BD Biosciences, CA, USA) and Annexin V conjugated to BV421 (BD Biosciences, CA, USA) to detect platelet EV expressing phosphatidylserine. Specificity of Annexin V binding to EV was tested by labeling in presence or absence of a calcium-chelator (20mM EDTA), as Annexin V requires calcium to bind to phosphatidylserine. To confirm the lipid nature of particles (EV) analyzed, EV were incubated with the non-ionic detergent Triton X-100 (0.2%). FCS files were analyzed using FlowJo software.

Preparation of human platelets
Venous blood (50 mL) was drawn from healthy subjects and COVID-19 patients, in accordance with guidelines of the Ethics Committee of Cheikh Zaïd Hospital of Rabat. Blood samples were anticoagulated in one-sixth volume of acid citrate dextrose (2.5 g of sodium citrate, 2 g of glucose, and 1.5 g of citric acid in 100 ml deionized water). The platelets were prepared in 30 mL plastic syringes containing 5 mL of ACD as anticoagulant as previously described.86,87 Platelet-rich plasma (PRP) was obtained by centrifugation of acid citrate dextrose (ratio of 1:5) anticoagulated blood at 200g for 15 minutes. Platelets were then pelleted from PRP (1000g for 10min), to which 1 µg/mL of PGE1 (Prostaglandin E1) was added, washed with HBSS-Hank’s sodium citrate buffer (138 mM NaCl, 5 mM KCl, 0.34 mM Na2HPO4, 0.4 mM KH2PO4, 4.2 mM Na2HCO3, 5.6 mM Glucose, 10 mM HEPES, 12.9 mM sodium citrate, pH 7.4), also containing PGE1 (0.5 µg/mL), and finally resuspended in HBSS-Hank’s buffer containing 2 mM MgCl2 and 2 mM CaCl2. Platelets were adjusted to a final concentration of 250 × 10^6/mL (for platelet aggregation assays) using an automated cell counter (CELL-DYN Ruby; Illinois, USA). The platelets were kept at 37°C for 30 min before further experiments. Platelet lysates were prepared at 500 × 10^6/mL using RIPA buffer and lysates were used to determine PF4, serotonin and cytokines as described above.

Platelet aggregation assay
Aggregation of washed platelets was monitored on an eight-channel optical aggregometer (SD Medical Innovation, Frouard, France). The samples (500 µL of the isolated platelet suspension) were stimulated or not with α-thrombin (Sigma Aldrich, USA) at concentrations of 0.025, 0.05 and 2 U/mL, under continuous stirring (1000 rpm) at 37°C. Platelet aggregation was then monitored following the addition of an appropriate concentration of α-thrombin and recorded until trace stabilization (or a maximum of 15 min) and light transmission was measured at the time of maximum aggregation.
**Rhodamine-based assay for platelet adhesion**

The relationship between the activation of platelets and the severity of COVID-19 was assessed in an ex-vivo perfusion system of human whole blood exposed to collagen-coated surfaces under flow. The ratio of activated platelets to total platelets (activated and non-activated platelet) was examined by double immunofluorescence using rhodamine-conjugated P-selectin antibody (activated platelet) and fluorescein isothiocyanate conjugated platelet membrane glycoprotein antibody (GPIIb/IIIa, total platelet). In brief, glass capillaries were coated overnight at 4°C with 250 µg/mL of fibrillar equine type 1 collagen (Chronolog). Two milliliters of sodium citrate anticoagulant were mixed with 200 µL of cell suspension (500 × 10^3) followed by incubation with rhodamine 6G (Sigma-Aldrich) for 15 min at 37°C. Stained samples were then perfused simultaneously in glass capillaries at a shear rate of 300/s for 5 min. After a washing step, images of the surfaces with adherent platelets were captured using a digital camera connected to a Nikon Eclipse NI-Motorized Microscope System (Plan 10x 0.25, Melville, NY, U.S). Platelet adhesion was quantified by morphometric analysis and platelet adhesion data were expressed as the percentage of capillary surface covered by platelets.

**Quantification of soluble factors derived from thrombin-activated platelets**

Platelet-rich plasma (PRP) was obtained by centrifugation of acid citrate dextrose (ratio of 1:5) anticoagulated blood at 200g for 15 minutes. Platelets were then pelleted from PRP, to which 1 µg/mL of PGE1 was added, washed with HBSS-Hank’s sodium citrate buffer (138 mM NaCl, 5 mM KCl, 0.34 mM Na2HPO4, 0.4 mM KH2PO4, 4.2 mM Na2HCO3, 5.6 mM Glucose, 10 mM HEPES, 12.9 mM sodium citrate, pH 7.4), also containing PGE1 (0.5 µg/mL), and finally resuspended in HBSS-Hank’s buffer containing 2 mM MgCl2 and 2 mM CaCl2. Washed human platelets were kept in a resting state (1 µg/mL of PGE1) or stimulated with α-thrombin (varying concentrations and time points). Supernatants were collected by centrifugation and platelet pellets were lysed with Triton buffer (1% Triton X-100, 0.05% Tween-20, 0.3 M NaCl and 1 mM phenylmethylsulfonyl fluoride (PMSF) in PBS). Samples were stored at −80°C until quantification of sCD40L, IL1β, IL-18 and thromboxane (TX) B2 (TXB2) (the stable metabolite of TXA2) levels using ELISA kits (R&D Systems) according to the manufacturer’s protocol.

**Immunoblotting**

Platelets isolated from healthy subjects, severe and non-severe COVID-19 patients were treated as follows: washed platelets were stimulated (or not) by 0.05 U/mL of α-thrombin for 5 min at room temperature. The reaction was stopped by the addition of an appropriate volume of 4x Laemmli buffer. Platelet lysates were analyzed by SDS-PAGE using antibodies against phospho-PKCδ Tyr311 (Cell Signaling Technology) and densitometry was determined using ImageJ. Membranes were stripped and blotted for GAPDH to evaluate protein loading (Santa Cruz Biotechnology).

**ACE2 detection by immunofluorescence**

Platelet from healthy controls were fixed in PFA 1% (10 volumes) for 60 min at room temperature and 500 000 platelets were centrifuged at 1200 g for 5 min on a
microscope slide. After a blocking step of 60 min at room temperature in PBS with 0.2% triton, 5% Normal Goat Serum (NGS) and 5% Normal Donkey Serum (NDS), platelets were incubated overnight at 4°C with a mouse anti-hCD41a antibody (Novus biological, clone M148 at 5 μg/mL) and a rabbit anti-ACE2 antibody (Thermofisher, clone SN0754 at 10 μg/mL) in PBS, 5% NGS and 5% NDS. After 3 washes with PBS, platelets were incubated with secondary antibodies: AF488-goat anti-mouse IgG (2.5 μg/mL, Thermofisher) and AF647-(Fab')2 donkey anti-rabbit IgG (2.5 μg/mL, Thermofisher) in PBS, 5% NGS and 5% NDS for 1h. A frozen section of fixed mouse kidney (7 μm) was used as a positive control for ACE2 in the same staining conditions. DAPI (1 μg/mL for 5 min) was used to stain the nuclei. Images were acquired at 40X with a Zeiss Inverted Axio Observer epifluorescence microscope (Zeiss, Germany) equipped with a Colibri 7 illumination source and an Axiocam 503 monochromatic camera (Axiocam MRm, Zeiss, Germany). ZEN software was used for image acquisition and processing (Zeiss, Germany). Optical sectioning was used to visualize 3 to 4 μm sections.

Quantification and Statistical analysis
Graph Pad Prism software (Version 8) was used for statistical analyses. Data were tested for outliers by ROUT method. Data were tested for normal distribution by Shapiro-Wilk test. Data that fit the assumption of normal distribution were compared using parametric analysis indicated in the respective figure legends: Student’s unpaired or paired t-test were used for comparing data from two groups. One-way ANOVA test with subsequent Sidak’s multiple comparisons test was used for multiple group data analysis. Data that did not fit the assumption of normal distribution were compared using non-parametric analysis indicated in the respective figure legends: Wilcoxon Mann Whitney Test for comparing data from two groups or Kruskal-Wallis test for comparing data from multiple groups with subsequent Dunn’s multiple comparisons test. Data are presented as mean ± SD or median with interquartile range (IQR). A P value of <0.05 was considered significant. P values higher than 0.1 are shown as NS. P values between 0.05 and 0.1 are displayed as numbers. ****P< 0.0001, ***P < 0.001, **P < 0.01 and *P < 0.05

The statistical analyses shown in Online Table VII and VIII and Table 2 and IX were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Kruskal-Wallis and Wilcoxon-Mann-Whitney tests were used to compare the distribution of laboratory parameters at admission between groups. Pearson correlation coefficients were calculated to study association of laboratory parameters with hospitalization time and time until patients identified negative for the virus (Table 2). These analyses (Table 2) did not include deceased patients, as some of these had a very short hospitalization time with no negative test results (i.e. for virus infection). The second set of correlations (Table 2) also excluded one patient who did not have a negative result (i.e. for virus infection) before leaving the hospital. A survival analysis was performed with a Cox Regression in Online Table IX.
## Online Tables

### Online Table I. Co-Morbidities.

| Index                                                                 | Total (n = 115) | Non-Severe (n = 71) | Severe (n = 44) |
|-----------------------------------------------------------------------|-----------------|---------------------|-----------------|
| N/A                                                                   | 52              | 33                  | 19              |
| Nothing to Report                                                     | 21              | 14                  | 7               |
| Allergy                                                               | 1               | 1                   | 0               |
| Android Obesity                                                       | 1               | 1                   | 0               |
| Arterial Hypertension                                                 | 3               | 2                   | 1               |
| Arterial Hypertension + Pulmonary Tuberculosis (2016)                 | 1               | 1                   | 0               |
| Asthma                                                                | 2               | 1                   | 1               |
| Asthma + Pericarditis                                                 | 1               | 1                   | 0               |
| Benign Prostatic Hyperplasia + Cardiopathy + Arterial Hypertension   | 1               | 0                   | 1               |
| Breast Cancer                                                         | 1               | 0                   | 1               |
| Breast Neoplasia + Immunosuppressed                                   | 1               | 1                   | 0               |
| Cardiopathy                                                           | 1               | 1                   | 0               |
| Cardiopathy + Hepatitis A + Smoker                                    | 1               | 1                   | 0               |
| Cardiopathy + Type 2 Diabetes                                         | 1               | 1                   | 0               |
| Cardiopathy + Type 2 Diabetes + Arterial Hypertension                 | 1               | 0                   | 1               |
| Cardiopathy + Type 2 Diabetes + Arterial Hypertension + COPD (chronic obstructive pulmonary disease) + Immunosuppressed + Cheek Cancer | 1               | 0                   | 1               |
| Chronic Inflammatory Arthritis                                        | 2               | 2                   | 0               |
| Endometrial Neoplasia                                                 | 1               | 1                   | 0               |
| Heart Valve Disease + Urolithiasis                                    | 1               | 1                   | 0               |
| Hodgkin Lymphoma                                                      | 1               | 1                   | 0               |
| Immunosuppressed                                                      | 1               | 1                   | 0               |
| Mental Health Disorder                                                | 1               | 1                   | 0               |
| Nephrotic Syndrome                                                    | 1               | 0                   | 1               |
| Parkinson’s Disease                                                   | 1               | 1                   | 0               |
| Pulmonary Abscess                                                     | 1               | 1                   | 0               |
| RALD (RAS-associated autoimmune leukoproliferative disorder)          | 1               | 1                   | 0               |
| Rheumatoid Arthritis                                                  | 1               | 0                   | 1               |
| Smoker                                                                | 2               | 1                   | 1               |
| Smoker + Cardiopathy                                                  | 1               | 1                   | 0               |
| Type 2 Diabetes                                                       | 4               | 2                   | 2               |
| Type 2 Diabetes + Arterial Hypertension                               | 3               | 1                   | 2               |
| Type 2 Diabetes + Open Heart Surgery (2019)                           | 1               | 1                   | 0               |
| Type 2 Diabetes + Pulmonary Metastases                                 | 1               | 0                   | 1               |
| Urinary System Disease                                                | 1               | 0                   | 1               |
### Online Table II. Medication (not related to COVID-19 treatment).

| Index                                      | Total (n = 115) | Non-Severe (n = 71) | Severe (n = 44) |
|--------------------------------------------|-----------------|---------------------|-----------------|
| N/A                                        | 91              | 59                  | 32              |
| Nothing to Report                          | 12              | 6                   | 6               |
| Anginib 100 mg                             | 1               | 1                   | 0               |
| Cardioaspirine + Co-apravit                | 1               | 0                   | 1               |
| Kardegic + Detensiel + Glucophage + Aprovax + Temesta | 1               | 1                   | 0               |
| Letrozole                                  | 1               | 1                   | 0               |
| Metformine + Cronodine + Sintrom           | 1               | 1                   | 0               |
| Metformine + Diamicron                     | 1               | 0                   | 1               |
| Metformine + Valsartan/Hydrochlorothiazide | 1               | 0                   | 1               |
| Methotrexate + Corticotherapy              | 2               | 2                   | 0               |
| Sintrom + Detensiel + Triatec              | 1               | 1                   | 0               |
| Vastarel + Coralan + ADO                   | 2               | 1                   | 1               |
| Ventolin                                   | 2               | 1                   | 1               |
| Index                  | Total (n = 115) | Non-Severe (n = 71) | Severe (n = 44) |
|-----------------------|-----------------|---------------------|-----------------|
| N/A                   | 4               | 2                   | 2               |
| Europe/ Jewish        | 1               | 0                   | 1               |
| Asian                 | 3               | 2                   | 1               |
| Middle East           | 7               | 5                   | 2               |
| North Africa/ Arabic  | 64              | 38                  | 26              |
| North Africa/ Berber  | 32              | 20                  | 12              |
| Europe/Spanish        | 5               | 5                   | 0               |
Online Table IV. Detection of SARS-CoV-2 in platelets. Related to Online Figure VI. ct = threshold cycle

| Index | Patients with COVID-19 |
|-------|------------------------|
|       | Healthy | Non-Severe | Severe |
| SARS-CoV-2 E gene | detection in platelets (positive/total donors) | 0/17 | 9/38 | 2/11 |
|       | ct values (mean ± SD) | n.d. | 28.89 ± 5.86 | 34 ± 2.82 |
Online Table V. Related to Online Table IV. Comparisons of Patients with SARS-CoV-2-associated platelets and SARS-CoV-2-free platelets

IQR = Interquartile Range; CRP = C-Reactive Protein; EV = Extracellular Vesicle; PF4 = Platelet Factor 4; PLR = Platelet-Lymphocyte Ratio; ALT = Alanine Transaminase; AST = Aspartate Transaminase; LDH = Lactate Dehydrogenase

* Statistical Analysis: Data were not normally distributed (Shapiro-Wilk test). Wilcoxon Mann Whitney Test to calculate \( P \) values.

| Parameter (on admission) | SARS-CoV-2 RNA associated with platelets | n | Median | IQR | *P-value |
|-------------------------|------------------------------------------|---|--------|-----|----------|
| Age, years              | Non-Severe: negative 29 41.00 (53.00-34.50) | 29 | 41.00 (53.00-34.50) | 9,75E-05 |
|                         | Non-Severe: positive 9 71.00 (74.50-57.00) | 9 | 71.00 (74.50-57.00) | N is too small |
|                         | Severe: negative 9 64.00 (41.00-37.00) | 9 | 64.00 (41.00-37.00) | N is too small |
|                         | Severe: positive 2 41.00 (74.00-8.00) | 2 | 41.00 (74.00-8.00) | N is too small |
| Weight, kg              | Non-Severe: negative 29 74.00 (91.00-59.00) | 29 | 74.00 (91.00-59.00) | 2.97E-01 |
|                         | Non-Severe: positive 9 65.00 (81.00-58.50) | 9 | 65.00 (81.00-58.50) | N is too small |
|                         | Severe: negative 9 70.00 (84.50-62.50) | 9 | 70.00 (84.50-62.50) | N is too small |
|                         | Severe: positive 2 66.00 (97.00-35.00) | 2 | 66.00 (97.00-35.00) | N is too small |
| Duration of hospitalization, days | Non-Severe: negative 29 14.00 (15.00-13.00) | 29 | 14.00 (15.00-13.00) | 7.12E-01 |
|                         | Non-Severe: positive 9 13.00 (19.00-13.00) | 9 | 13.00 (19.00-13.00) | N is too small |
|                         | Severe: negative 9 23.00 (28.00-14.50) | 9 | 23.00 (28.00-14.50) | N is too small |
|                         | Severe: positive 2 27.50 (35.00-20.00) | 2 | 27.50 (35.00-20.00) | N is too small |
| Platelet value at admission, \( \times 10^6 \)/mL | Non-Severe: negative 29 207.0 (298.0-163.0) | 29 | 207.0 (298.0-163.0) | 1.26E-01 |
|                         | Non-Severe: positive 9 156.0 (235.5-105.0) | 9 | 156.0 (235.5-105.0) | N is too small |
|                         | Severe: negative 9 97.0 (224.5-73.0) | 9 | 97.0 (224.5-73.0) | N is too small |
|                         | Severe: positive 2 73.5 (115.0-32.0) | 2 | 73.5 (115.0-32.0) | N is too small |
| Lymphocyte value at admission, \( \times 10^6 \)/mL | Non-Severe: negative 29 1.08 (1.44-0.83) | 29 | 1.08 (1.44-0.83) | 6.67E-01 |
|                         | Non-Severe: positive 9 0.98 (1.39-0.73) | 9 | 0.98 (1.39-0.73) | N is too small |
|                         | Severe: negative 9 1.13 (1.19-0.45) | 9 | 1.13 (1.19-0.45) | N is too small |
|                         | Severe: positive 2 0.84 (0.88-0.80) | 2 | 0.84 (0.88-0.80) | N is too small |
| Platelet-Lymphocyte Ratio at admission | Non-Severe: negative 29 182.9 (298.9-125.4) | 29 | 182.9 (298.9-125.4) | 4.78E-01 |
|                         | Non-Severe: positive 9 138.3 (199.7-128.0) | 9 | 138.3 (199.7-128.0) | N is too small |
|                         | Severe: negative 9 154.8 (242.3-65.07) | 9 | 154.8 (242.3-65.07) | N is too small |
|                         | Severe: positive 2 85.34 (130.7-40.00) | 2 | 85.34 (130.7-40.00) | N is too small |
| ALT value at admission, U/L | Non-Severe: negative 29 36.40 (49.05-21.00) | 29 | 36.40 (49.05-21.00) | 2.89E-01 |
|                         | Non-Severe: positive 9 30.20 (48.35-13.60) | 9 | 30.20 (48.35-13.60) | N is too small |
|                         | Severe: negative 9 28.50 (45.40-22.00) | 9 | 28.50 (45.40-22.00) | N is too small |
|                         | Severe: positive 2 38.35 (42.10-34.60) | 2 | 38.35 (42.10-34.60) | N is too small |
| Parameter                              | Non-Severe: negative | Non-Severe: positive | Severe: negative | Severe: positive |
|---------------------------------------|----------------------|----------------------|------------------|------------------|
| **AST value at admission, U/L**      | 29 45.20 (52.80-29.45) | 9 37.20 (53.90-16.65) | 9 25.60 (45.40-23.35) | 2 50.55 (55.30-45.80) |
|                                       |                      | 9 37.20 (53.90-16.65) | 2 50.55 (55.30-45.80) |                  |
| **LDH value at admission, U/L**      | 29 401.0 (679.5-255.0) | 9 506.0 (708.5-361.5) | 9 650.0 (794.5-485.0) |                  |
|                                       |                      | 9 506.0 (708.5-361.5) | 9 650.0 (794.5-485.0) |                  |
| **D-Dimers value at admission, mg/L**| 29 0.66 (1.11-0.39)   | 9 0.67 (1.09-0.39)    | 9 0.89 (1.23-0.53)  |                  |
|                                       |                      | 9 0.67 (1.09-0.39)    | 9 0.89 (1.23-0.53)  |                  |
| **CRP value at admission, mg/L**     | 29 4.270 (10.09-1.45) | 9 9.50 (15.36-4.33)   | 9 15.78 (28.98-5.61) |                  |
|                                       |                      | 9 9.50 (15.36-4.33)   | 9 15.78 (28.98-5.61) |                  |
| **CD41+ EV, EV/ml (x10^8)**          | 29 1.95 (2.64-1.56)   | 9 2.13 (2.52-1.48)    | 9 1.27 (1.32-1.22)  |                  |
|                                       |                      | 9 2.13 (2.52-1.48)    | 9 1.27 (1.32-1.22)  |                  |
| **AnnexinV+CD41+ EV, EV/mL (x10^8)** | 29 0.86 (1.45-0.37)   | 9 0.31 (1.49-0.22)    | 9 0.32 (0.34-0.15)  |                  |
|                                       |                      | 9 0.31 (1.49-0.22)    | 9 0.32 (0.34-0.15)  |                  |
| **PF4 in Plasma, ng/mL**              | 29 11917 (18465-8779) | 9 11213 (19068-9463)  | 9 13416 (16501-11537) |                  |
|                                       |                      | 9 11213 (19068-9463)  | 9 13416 (16501-11537) |                  |
| **Serotonin in Plasma, ng/mL**       | 29 171.0 (282.0-141.0) | 9 147.0 (338.5-128.0) | 9 167.0 (258.0-68.0) |                  |
|                                       |                      | 9 147.0 (338.5-128.0) | 9 167.0 (258.0-68.0) |                  |
Online Table VI. Pearson Correlation of Extracellular Vesicles with Platelet Values (N=115)

EV = Extracellular Vesicle

| Parameter (on admission) | Platelet Value |  
|-------------------------|----------------|
|                         | $r$ | $P$-value |
| CD41+ EV                | 0.19 | 4.20E-02 |
| AnnexinV+CD41+ EV       | 0.09 | 3.40E-01 |
Online Table VII. Comparison of clinical parameters between self-identified ethnic groups.

IQR = Interquartile Range; CRP = C-Reactive Protein; EV = Extracellular Vesicle; PF4 = Platelet Factor 4; PLR = Platelet-Lymphocyte Ratio; ALT = Alanine Transaminase; AST = Aspartate Transaminase; LDH = Lactate Dehydrogenase

* Based on Kruskal Wallis test.

| Parameter (on admission) | Ethnicity            | n  | Median        | IQR           | P-value       |
|--------------------------|----------------------|----|---------------|---------------|---------------|
| D-Dimers, mg/L           | Asian                | 3  | 0.59          | (0.87-0.50)   | 4.04E-01      |
|                          | Europe/Spanish       | 5  | 1.12          | (1.15-0.67)   |               |
|                          | Middle East          | 7  | 0.61          | (1.05-0.31)   |               |
|                          | North Africa/Arab    | 64 | 0.72          | (1.06-0.45)   |               |
|                          | North Africa/Berber  | 32 | 0.54          | (1.11-0.35)   |               |
| CRP, mg/L                | Asian                | 3  | 16.52         | (36.42-1.15)  | 6.86E-01      |
|                          | Europe/Spanish       | 5  | 6.87          | (13.27-2.14)  |               |
|                          | Middle East          | 7  | 6.31          | (36.7-41.43)  |               |
|                          | North Africa/Arab    | 64 | 7.06          | (17.16-3.47)  |               |
|                          | North Africa/Berber  | 32 | 13.88         | (29.05-5.20)  |               |
| CD41+ EV, EV/mL (x10^8)  | Asian                | 3  | 2.53          | (7.38-1.16)   | 2.25E-01      |
|                          | Europe/Spanish       | 5  | 0.94          | (1.1-0.59)    |               |
|                          | Middle East          | 7  | 1.31          | (1.45-1.26)   |               |
|                          | North Africa/Arab    | 64 | 1.55          | (2.48-1.02)   |               |
|                          | North Africa/Berber  | 32 | 1.67          | (2.75-1.24)   |               |
| AnnexinV+CD41+ EV, EV/mL (x10^8) | Asian | 3 | 167101881  | (6.47-0.59) | 2.30E-01 |
|                          | Europe/Spanish       | 5  | 0.312         | (0.88-0.76)   |               |
|                          | Middle East          | 7  | 0.34          | (0.37-0.33)   |               |
|                          | North Africa/Arab    | 64 | 0.47          | (1.26-0.17)   |               |
|                          | North Africa/Berber  | 32 | 0.77          | (1.39-0.23)   |               |
| PF4 in Plasma, ng/mL     | Asian                | 3  | 9698.47       | (10652.70-9338.91) | 2.63E-01 |
|                          | Europe/Spanish       | 5  | 1775.51       | (9523.51-1093.64) |               |
|                          | Middle East          | 7  | 10456.93      | (12640.00-8634.53) |               |
|                          | North Africa/Arab    | 64 | 12413.25      | (15692.26-8920.37) |               |
|                          | North Africa/Berber  | 32 | 11625.00      | (17270.98-8495.95) |               |
| Serotonin in Plasma, ng/mL | Asian          | 3  | 251.48        | (279.68-191.40) | 8.17E-01 |
|                          | Europe/Spanish       | 5  | 101.72        | (278.83-87.65) |               |
|                          | Middle East          | 7  | 150.40        | (220.55-137.69) |               |
|                          | North Africa/Arab    | 63 | 166.26        | (295.48-97.53) |               |
|                          | North Africa/Berber  | 32 | 183.80        | (294.80-97.21) |               |
| Platelets/mL, (x10^6)    | Asian                | 3  | 162.00        | (556.00-156.00) | 7.70E-01 |
|                          | Europe/Spanish       | 5  | 127.00        | (299.00-105.00) |               |
|                          | Middle East          | 7  | 174.00        | (289.00-94.00) |               |
|                          | North Africa/Arab    | 64 | 175.50        | (214.00-112.50) |               |
| Region                  | Count | Mean   | Range       |
|------------------------|-------|--------|-------------|
| North Africa/Berber    | 32    | 136.50 | (247.50-87.00) |
| Lymphocytes/mL, (x10^6) |       |        |             |
| Asian                  | 3     | 1.17   | (1.18-0.57) |
| Europe/Spanish         | 5     | 1.09   | (1.50-0.45) |
| Middle East            | 7     | 1.08   | (1.43-0.39) |
| North Africa/Arab      | 64    | 1.12   | (1.50-0.79) |
| North Africa/Berber    | 32    | 1.03   | (1.59-0.68) |
| PLR                    |       |        |             |
| Asian                  | 3     | 284.21 | (471.19-133.33) |
| Europe/Spanish         | 5     | 225.28 | (282.22-199.33) |
| Middle East            | 7     | 190.40 | (429.09-121.68) |
| North Africa/Arab      | 64    | 151.75 | (265.29-102.47) |
| North Africa/Berber    | 32    | 124.72 | (195.36-74.04) |
| ALT, U/L               |       |        |             |
| Asian                  | 3     | 31.40  | (46.50-14.80) |
| Europe/Spanish         | 5     | 15.80  | (34.80-15.00) |
| Middle East            | 7     | 41.50  | (47.20-17.50) |
| North Africa/Arab      | 64    | 36.40  | (46.20-26.40) |
| North Africa/Berber    | 32    | 31.40  | (46.00-22.85) |
| AST, U/L               |       |        |             |
| Asian                  | 3     | 22.80  | (46.00-14.90) |
| Europe/Spanish         | 5     | 19.20  | (61.50-15.00) |
| Middle East            | 7     | 34.70  | (46.70-19.00) |
| North Africa/Arab      | 64    | 45.20  | (55.45-31.10) |
| North Africa/Berber    | 32    | 44.15  | (57.70-26.25) |
| LDH, U/L               |       |        |             |
| Asian                  | 3     | 441.00 | (482.00-202.00) |
| Europe/Spanish         | 5     | 640.00 | (854.00-524.00) |
| Middle East            | 7     | 779.00 | (857.00-276.00) |
| North Africa/Arab      | 64    | 579.50 | (807.00-378.00) |
| North Africa/Berber    | 32    | 528.50 | (744.50-270.50) |
Online Table VIII. Comparison of clinical parameters between sexes.

IQR = Interquartile Range; CRP = C-Reactive Protein; EV = Extracellular Vesicle; PF4 = Platelet Factor 4; PLR = Platelet-Lymphocyte Ratio; ALT = Alanine Transaminase; AST = Aspartate Transaminase; LDH = Lactate Dehydrogenase

* Based on Wilcoxon Mann Whitney Test.

| Parameter (on admission) | Sex (F/M) | n | Median | IQR | *P-value |
|--------------------------|-----------|---|--------|-----|----------|
| D-Dimers, mg/L           | F         | 50| 0.83   | (1.07-0.46) | 5.54E-02 |
|                          | M         | 65| 0.56   | (1.09-0.36) |          |
| CRP, mg/L                | F         | 50| 7.90   | (26.47-3.18) | 8.81E-01 |
|                          | M         | 65| 7.49   | (16.52-4.27) |          |
| CD41+ EV, EV/mL (x10^8)  | F         | 50| 1.46   | (2.34-1.16)  | 7.81E-01 |
|                          | M         | 65| 1.59   | (2.53-1.06)  |          |
| AnnexinV+CD41+ EV, EV/mL (x10^8) | F | 50| 0.39   | (1.22-0.22)  | 6.27E-01 |
|                          | M         | 65| 0.59   | (1.34-0.21)  |          |
| PF4 in Plasma, ng/mL     | F         | 50| 10932.98 | (14811.00-8634.53) | 3.05E-01 |
|                          | M         | 65| 11565.76 | (17381.59-8556.89) |          |
| Serotonin in Plasma, ng/mL | F   | 50| 168.05 | (278.83-97.53) | 7.05E-01 |
|                          | M         | 64| 165.02 | (296.12-113.59) |          |
| Platelets/mL, (x10^6)    | F         | 50| 156.50 | (233.00-106.00) | 4.31E-01 |
|                          | M         | 65| 180.00 | (236.00-115.00) |          |
| Lymphocytes/mL, (x10^6)  | F         | 50| 1.09   | (1.51-0.64)  | 8.99E-01 |
|                          | M         | 65| 1.05   | (1.49-0.60)  |          |
| PLR                      | F         | 50| 150.84 | (258.10-102.05) | 9.69E-01 |
|                          | M         | 65| 147.01 | (282.35-100.77) |          |
| ALT, U/L                 | F         | 50| 32.40  | (41.70-19.60)  | 1.39E-01 |
|                          | M         | 65| 36.40  | (46.70-28.50)  |          |
| AST, U/L                 | F         | 50| 35.70  | (50.20-21.50)  | 1.43E-01 |
|                          | M         | 65| 45.60  | (55.60-33.20)  |          |
| LDH, U/L                 | F         | 50| 549.00 | (786.00-401.00) | 9.60E-01 |
|                          | M         | 65| 576.00 | (765.00-297.00) |          |
### Online Table IX. Comparison of Clinical Parameters (on admission) between survivors and non-survivors.

IQR = Interquartile Range; CRP = C-Reactive Protein; EV = Extracellular Vesicle; PF4 = Platelet Factor 4; PLR = Platelet-Lymphocyte Ratio; ALT = Alanine Transaminase; AST = Aspartate Transaminase; LDH = Lactate Dehydrogenase

| Parameter (on admission) | Survivor/Non-Survivor | n | Median | IQR         | Hazard Ratio (95% CI) ‡ | *P-value |
|--------------------------|-----------------------|---|--------|-------------|-------------------------|----------|
| Age, years               | **Survivor**          | 110 | 50     | 68-38.25    | 1.1 (1.03;1.17)         | 3.90E-03 |
|                          | **Non-Survivor**      | 5  | 70     | 98-69       |                         |          |
| Weight, kg               | **Survivor**          | 109† | 76     | 89-64       |                         | 1 (0.93; 1.07) | 9.1E-01 |
|                          | **Non-Survivor**      | 3†  | 87     | 87.5-72.5   |                         |          |
| D-Dimers, mg/L (multiplied by 10) | **Survivor**      | 110 | 6.30 | (10.15-4.10) | 1.35(1.17;1.57)         | 7.1E-05  |
|                          | **Non-Survivor**      | 5  | 24.50 | (25.50-19.00) |                         |          |
| CRP, mg/L                | **Survivor**          | 110 | 7.30  | (18.41-3.50) | 1.09(1.03;1.17)         | 6.8E-03  |
|                          | **Non-Survivor**      | 5  | 45.85 | (47.27-31.62)|                         |          |
| CD41+ EV, EV/mL (divided by 10³) | **Survivor**      | 110 | 1.56 | (2.43-1.12) |                         |          |
|                          | **Non-Survivor**      | 5  | 0.59  | (1.06-0.51)  |                         |          |
| AnnexinV+CD41+ EV, EV/mL (divided by 10⁷) | **Survivor**      | 110 | 5.17 | (13.40-2.21) |                         |          |
|                          | **Non-Survivor**      | 5  | 2.90  | (3.13-2.16)  |                         |          |
| PF4 in Plasma, ng/mL (divided by 10³) | **Survivor**      | 110 | 1.14 | (1.58-0.86) |                         |          |
|                          | **Non-Survivor**      | 5  | 0.95  | (1.29-0.81)  |                         |          |
| Serotonin in Plasma, ng/mL | **Survivor**      | 109 | 163.79 | (288.67-103.42) |                         |          |
|                          | **Non-Survivor**      | 5  | 249.27 | (294.85-178.32) |                         |          |
| Platelets/mL, (x10⁶)     | **Survivor**          | 110 | 174.00 | (236.00-112.00) |                         |          |
|                          | **Non-Survivor**      | 5  | 90.00 | (105.00-83.00) |                         |          |
| Lymphocytes/mL, (x10⁶)   | **Survivor**          | 110 | 1.09  | (1.50-0.64)  |                         |          |
|                          | **Non-Survivor**      | 5  | 0.38  | (1.14-0.36)  |                         |          |
| PLR                      | **Survivor**          | 110 | 150.84 | (273.33-102.05) |                         |          |
|                          | **Non-Survivor**      | 5  | 76.32 | (291.67-72.81)|                         |          |
| ALT, U/L                 | **Survivor**          | 110 | 35.00 | (46.20-23.40) |                         |          |
|                          | **Non-Survivor**      | 5  | 36.40 | (39.50-23.90) |                         |          |
| AST, U/L                 | **Survivor**          | 110 | 44.15 | (55.30-24.50) |                         |          |
|                          | **Non-Survivor**      | 5  | 39.70 | (61.50-38.10) |                         |          |
| LDH, [U/L] (divided by 100) | **Survivor**      | 110 | 5.40  | (7.55-2.97) |                         |          |
|                          | **Non-Survivor**      | 5  | 9.85  | (11.53-9.82) |                         |          |

* Based on Cox Regression with 95% Wald confidence interval
† Weight (kg) data not available for 3 patients
‡ For the purpose of representing Hazard Ratios, certain values were multiplied/divided: D-Dimers, mg/mL (multiplied by 10); CD41+ EV, EV/mL (divided by 10³); Annexin-
V+CD41+ EV, EV/mL (divided by 10^7); PF4 in Plasma, ng/mL (divided by 10^3); LDH, U/L (divided by 100).
Online Table X. Pearson Correlation of D-Dimers with Platelet Markers (N=115)
EV = Extracellular Vesicle; PF4 = Platelet factor 4; CRP = C-reactive Protein; LDH = Lactate Dehydrogenase

| Parameter (on admission) | D-Dimers | | CRP | | LDH |
|--------------------------|----------|---------------|----------|---------------|----------|
|                          | $r$      | $P$-value     | $r$      | $P$-value     | $r$      | $P$-value |
| Platelet value           | -0.09    | 3.18E-01      | -0.24    | 8.80E-03      | -0.35    | 2.00E-04  |
| CD41+ EV                 | -0.16    | 9.29E-02      | -0.19    | 4.01E-02      | -0.27    | 4.00E-03  |
| AnnexinV+CD41+ EV        | -0.17    | 6.78E-02      | -0.17    | 6.20E-02      | -0.21    | 2.56E-02  |
| PF4 in Plasma            | 0.05     | 5.85E-01      | -0.09    | 2.88E-01      | -0.12    | 1.92E-01  |
| Serotonin in Plasma      | 0.04     | 6.72E-01      | 0.08     | 4.02E-01      | -0.04    | 6.47E-01  |
Online Figure I. Patient enrolment flow chart for the study. SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, RT-PCR = real time–polymerase chain reaction, COVID-19 = coronavirus disease 2019.
Online Figure II. Thoracic computed tomography imaging of a confirmed case of COVID-19 with typical findings and its respective report. Patients with a recent history of fever, shortness of breath, and desaturation were admitted to the hospital. Thoracic computed tomography (CT) and nasopharyngeal swabs (RT-PCR) confirmed the COVID-19 infection. (A) Healthy control; (B) COVID-19 patient (red arrow: infectious nodules).
Online Figure III. Related to Table 1. Representative real-time PCR quantification of SARS-CoV-2 RNA in throat swabs. 1: positive control; 2, 3, 4 and 5: patients with COVID-19; 6: no template control; 7: patient with negative RT-PCR.
Online Figure IV. Related to Table 1. Clinical analysis and blood parameters of COVID-19 patients. Age, duration of hospitalization, weight, thrombocytopenia, lymphopenia, inflammation markers (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate Dehydrogenase (LDH) and C-reactive Protein (CRP)) and D-Dimers were compared between COVID-19 non-severe (n=71) and COVID-19 severe (n=44) patients. Normal ranges (according
to the Medical Council of Canada) are indicated with dotted lines for each parameter. Data are represented as median with interquartile range (IQR). Statistical analysis: Data were not normally distributed (Shapiro-Wilk test). Wilcoxon Mann Whitney Test. *P<0.05, **P<0.01 and ****P<0.0001.
Online Figure V. Related to Table 1. Clinical analysis and blood parameters of COVID-19 patients, comparisons of Survivors and Non-Survivors. Age, duration of hospitalization, weight, thrombocytopenia, lymphopenia, inflammation markers (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate Dehydrogenase (LDH) and C-reactive Protein (CRP)) and D-Dimers were compared between COVID-19 non-severe (n=71, survivors), COVID-19 severe (n=39, survivors) and COVID-19 non-survivors (n=5) patients. Normal ranges (according to the Medical Council of Canada) are indicated with dotted lines for each parameter.
Data are represented as median with interquartile range (IQR). Statistical analysis: Data were not normally distributed (Shapiro-Wilk test). Kruskal-Wallis test with subsequent Dunn's multiple comparisons test. *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001.
Online Figure VI. Related to Table 2. Real-time PCR quantification of SARS-CoV-2 in platelets. Amplification curves for healthy controls, COVID-19 non-severe and COVID-19 severe patients are represented. Representative amplification curves of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).
Online Figure VII. Related to Figure 1 and Figure 2B. Plasma and platelet content in cytokines and chemokines. Cytokines and chemokines (48 in total) were evaluated either in the plasma of healthy controls (n=10), COVID-19 non-severe (n=10) and severe (n=9) or in the platelet content of healthy controls (n=9), COVID-19 non-severe (n=10) and severe (n=9). Data are represented as median with interquartile range (IQR). Statistical analysis: Data were not normally distributed (Shapiro-Wilk test). Kruskal-Wallis test with subsequent Dunn’s multiple comparisons test. *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001.
Online Figure VIII

A

silica beads

B

Annexin V

control +EDTA +Triton X-100

control +EDTA +Triton X-100

CD41+ EV

0.1μm 1μm 1μm

0.1μm 0.1μm 0.1μm

FSC PMT-H

FSC PMT-H

SSC-H

SSC-H

CD41+ (%)

NS

100 100

control +EDTA control +Triton X-100

Annexin V+ CD41+ EV

Annexin V+ CD41+ EV

Annexin V+ CD41+ EV

FSC PMT-H

FSC PMT-H

SSC-H

SSC-H

CD41

0.1μm 1μm 1μm

0.1μm 0.1μm 0.1μm

control +EDTA control +Triton X-100

Annexin V+ CD41+ (%)

100 100

control +EDTA control +Triton X-100

* * * * *
Online Figure VIII. Related to Figure 4. Validation of platelet EV detection by flow cytometry analysis. Silica beads (diameter 0.1µm, 0.5µm and 1µm) were used to define a gate size that includes only extracellular vesicles (EV). Gating strategy for the detection of CD41+ EV (A) or for the detection of Annexin V+ CD41+ EV (B). Plasma was incubated with 0.2% Triton-X100 to validate membrane moiety of the EV (n=3) or with EDTA 20mM to confirm the specificity of Annexin V binding (n=3). Scatter plots are representative of each condition (Control; +EDTA; +Triton X-100) and for all EV-analysis. FSC=forward scatter, SSC=sideward scatter. Data are represented as mean ± SD. Statistical analysis: paired T-test. **P<0.01 and ***P<0.001.
Online Figure IX. Related to Figure 4. Platelet extracellular vesicle numbers normalized to platelet values. Circulating platelet extracellular vesicles (CD41+ EV) expressing phosphatidylserine or not analyzed in plasma from healthy controls (n=18), COVID-19 non-severe (n=71) and COVID-19 severe patients (n=44) (see Figure 4) were normalized to platelet values (number of platelets/mL). Data are represented as median with interquartile range (IQR). Statistical analysis: Data were not normally distributed (Shapiro-Wilk test). Kruskal-Wallis test with subsequent Dunn’s multiple comparisons test.
Online Figure X

A  Healthy  COVID-19, non-severe  COVID-19, severe
Detection of ACE-2 RNA
human ACE2 PrimePCR Probe Assay, Human

Detection of genomic DNA
PrimePCR DNA Contamination Control
Probe Assay, Human

B  Healthy  COVID-19, non-severe  COVID-19, severe  Melting curve
Detection of ACE-2 RNA
intron-spanning primers

C  Kidney  Platelets
ACE 2
DAPI  ACE 2  CD41

Scale bar
Online Figure X. ACE2 expression in platelets. A-C) Real-time PCR quantification of ACE2 mRNA or genomic DNA in platelets from healthy controls (n=4), COVID-19 non-severe (n=4) or COVID-19 severe patients (n=3). Samples (n=11) isolated from enriched platelets (97.04±1.29%). A) Amplification curves of ACE2 RNA using intron-spanning primers (SYBR Green) and RNA from HaCat cells was used as a positive control. Melting curves obtained for the different amplifications are illustrated in the right panel. B) Amplification curves of ACE2 from the same samples using non-intron spanning primers (Taqman): human ACE2 PrimePCR Probe Assay (BioRad, CA, USA). C) Amplification curves of genomic DNA control sequences from the same samples using: PrimePCR DNA Contamination Control Probe Assay, Human (BioRad, CA, USA). D) ACE2 (red) was detected by immunofluorescence in kidney section from mice as a positive control (left panel). Nuclear staining (DAPI) is shown in blue. Resting platelets from healthy controls (right panel) were incubated with anti-CD41 (green) and anti-ACE2 (red) antibodies, scale bar 20 μm, images are representative of 3 healthy controls. Images were acquired at 40X with a Zeiss Inverted Axio Observer epifluorescence microscope (Zeiss, Germany) equipped with a Colibri 7 illumination source and an Axiocam 503 monochromatic camera (Axiocam MRm, Zeiss, Germany).