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RESEARCH ARTICLE

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Complete blood count, coagulation biomarkers, and lung function 6 months after critical COVID-19

Salla Kattainen[1] | Hanna Pitkänen[1] | Jere Reijula[2] | Johanna Hästbacka[3]

[1]Division of Intensive Care, Department of Perioperative and Intensive Care Medicine, University of Helsinki and HUS Helsinki University Hospital, Helsinki, Finland

[2]Department of Pulmonology, Heart and Lung Center, University of Helsinki and HUS Helsinki University Hospital, Helsinki, Finland

[3]Department of Anaesthesia and Intensive Care, Tampere University Hospital, University of Tampere, Tampere, Finland

Correspondence
Salla Kattainen, Intensive Care Unit, Meilahti Bridge Hospital, Haartmaninkatu 4, 00290 Helsinki, Finland.
Email: salla.kattainen@hus.fi

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Abstract

Background: Understanding the recovery of post-COVID-19 organ dysfunction is essential.

We evaluated coagulation 6 months post-COVID-19, examining its recovery and association with lung function.

Methods: Patients treated for COVID-19 at intensive care units between 3/2020 and 1/2021 were analyzed for complete blood count (CBC) and coagulation biomarkers (prothrombin time activity (%) (PT%), activated partial thromboplastin time (APTT), fibrinogen, coagulation factor VIII (FVIII), antithrombin (AT), and D-dimer) during the 6 months post-hospitalization. Results were compared with acute phase values and correlated with pulmonary function tests (PFT), including forced vital capacity (FVC) and hemoglobin-corrected diffusing capacity percentage of predicted (DLCOc%), recorded 6 months post-hospitalization. We examined the association between coagulation biomarkers and DLCOc% using linear regression with age, sex, and invasive mechanical ventilation (IMV) duration, and FVIII (correlated with DLCOc %) as covariates.

Results: Most CBCs and coagulation biomarkers had median values within the normal range. However, only 21% (15/70) of patients achieved full normalization of all biomarkers. Compared to acute COVID-19, hemoglobin, PT%, and AT increased, while leukocytes, fibrinogen, FVIII, and D-dimer decreased. Despite decreased levels, FVIII remained elevated in 46% (31/68), leukocytes in 26% (18/70), and D-dimer in 27% (18/67) at 6 months. A weak negative correlation ($r = -0.37$, $p = .036$) was found between DLCOc% and FVIII. Multivariable analysis revealed a weak, independent association between DLCOc% and FVIII. Excluding patients with anticoagulation therapy, FVIII no longer correlated with DLCOc%, while AT showed a moderate correlation with DLCOc%.

Conclusion: Only a few patients had normal CBC and coagulation biomarker values 6 months after critical COVID-19. A weak negative correlation between DLCOc%

and FVIII suggests that deranged coagulation activity may be associated with reduced diffusing capacity.

KEYWORDS
coagulation, COVID-19, critical care, lung function, PASC

Editorial Comment

In a small cohort of survivors of Covid-19, examined 5–6 months after intensive care, there was a weak association between elevated factor VIII in blood and impaired pulmonary diffusing capacity for carbon monoxide, supporting the idea that disturbed coagulation may be linked to lung injury in SARS-CoV-2 infection.

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome virus (SARS-CoV-2), is mainly associated with mild respiratory symptoms, but in critical cases, respiratory failure, progressive coagulopathy, and multi-organ failure necessitate intensive care.[1,2] After critical disease, many COVID-19 survivors suffer from persistent, recurrent, or new symptoms several months after recovery from acute infection.[3] This phenomenon, called post-acute sequelae of SARS-CoV-2 (PASC) or long COVID, affects up to 40% of COVID-19 survivors globally.[4] The consequences following COVID-19 include both pulmonary and extrapulmonary symptoms.[5,6] These symptoms result from an immunological imbalance, endothelial injury, and activation of coagulation, often accompanied by thromboembolism.[5,7] This combination can impair gas exchange in the lungs[8] and may even contribute to post-COVID interstitial lung disease (PC-ILD).[9] Furthermore, hypoxia resulting from COVID-19 may trigger a prothrombotic state. Conversely, the mechanisms of altered coagulation contribute to hypoxia, which, in turn, promotes the thrombo-inflammatory loop.[10] In addition to pulmonary symptoms, impaired lung function, abnormalities in lung imaging, and even fibrosis are reported up to 1 year after the initial disease.[3]

In association with the acute phase of COVID-19 disease, the rate of thromboembolic events is enhanced compared with other pulmonary infections.[11] In severe disease, neutrophils are prone to release neutrophil extracellular traps (NETs).[12] Enhanced tissue factor expression, platelet activation, and subsequent NETosis (NETinjury) events are associated with endothelial damage and loss of regulatory pathways of coagulation and fibrinolysis induce non-overt and overt thrombosis.[12,13] In addition to the coagulation abnormalities in the acute phase, reports have shown their persistence in the recovery phase.[14] These thrombo-inflammatory findings occur mainly in patients with acute severe illness,[14,15] but are also associated with long-lasting symptoms affecting outpatients.[6,16]

Our aim was to assess complete blood count (CBC) and coagulation biomarkers at 6 months after hospitalization for critical COVID-19, observing their recovery from the acute phase. Additionally, we aimed to evaluate the association of coagulation biomarkers with pulmonary function parameters (forced vital capacity [FVC] and diffusing capacity percentage of predicted [DLCOc%]) 6 months after COVID-19. The primary objective was to assess the CBC and coagulation biomarkers at 6 months post-hospitalization. We hypothesized that coagulation activity would not be normalized by the 6-month follow-up (FU), and that CBC and coagulation biomarkers would be associated with pulmonary function.

2 | METHODS

This study is an observational post hoc sub-study of a prospective RECOVID study registered in ClinicalTrials.gov (NCT04864938) and reporting accords with STROBE guidelines[17] (Supplementary Table 1). The RECOVID study investigates long-term recovery from COVID-19 in different severity groups. The Ethics Board of Helsinki University Hospital (HUS/1949/2020) approved the study protocol and amendments, which all follow the Good Clinical Practice. All participants gave written informed consent prior to participating in the study. The patients were free to choose in which parts of the study they wanted to participate, including the use of their clinical data from the periods of hospitalization and FU. A detailed description of the long-term lung function, including results of spirometry, diffusing capacity, six-minute walk test, and lung x-ray results of patients admitted to intensive care units (ICUs) has been previously published.[18]

2.1 | Study population

All consecutive eligible patients with a laboratory-confirmed (positive SARS-CoV-2-polymerase chain reaction test or seropositivity) COVID-19 treated in ICUs at the Helsinki University Hospital District between March 2020 and January 2021 were invited to participate the study (Figure 1). We identified eligible patients after hospital discharge using the international classification of diseases (ICD-10) code U07.1 (laboratory-confirmed SARS-CoV-2 infection) as the primary diagnosis, and with the COVID-19 detached data collection operated by the Finnish intensive care quality register.[19] The inclusion criteria for this study were age ≥18 years and Finnish as the primary language. Patients with major prior neurological diseases such as

Parkinson's disease, progressive memory disorder, traumatic brain injury, major stroke, severely impaired hearing or vision, and developmental disability, were not included, as these conditions were exclusion criteria in the RECOVID study, which focused on neuropsychological recovery after critical COVID-19.[20] We also excluded pregnant patients.

2.2 | Data collection

We extracted clinical data concerning the hospitalization, including demographic data, medical history, and prior anticoagulant therapy. This encompassed CBC and coagulation biomarkers (prothrombin time activity [%] [PT%], activated partial thromboplastin time [APTT], fibrinogen, coagulation factor VIII [FVIII], antithrombin [AT], and D-dimer). Information on hospital treatment modalities, such as invasive mechanical ventilation (IMV), prone positioning, and pharmacological treatment (antibiotics, oseltamivir, remdesivir, hydroxychloroquine, corticosteroids, enoxaparin) was also recorded. Additionally, we documented anticoagulant therapy at FU, and chest CT scans performed on clinical indication between hospital discharge and FU. The data were sourced from electronic medical records (Epic™, Verona, US, Uranus™, CGI, Montreal, Canada, PICIS™, Wakefield, US). The data on pre-existing diseases relied on the ICD-10 diagnoses as outlined in the medical records. Information regarding smoking habits was gathered from medical records during the acute treatment period for COVID-19. The pharmacological treatment during the hospitalization for COVID-19 included medications administered both before and during the ICU admission.

Patients were invited to a clinical and research FU visit, where a trained intensivist interviewed them 6 months after hospital discharge. The patients underwent plasma sampling for CBC and coagulation laboratory assessment, and pulmonary function tests (PFT) (spirometry and diffusing capacity). Results regarding lung function have been published.[18]

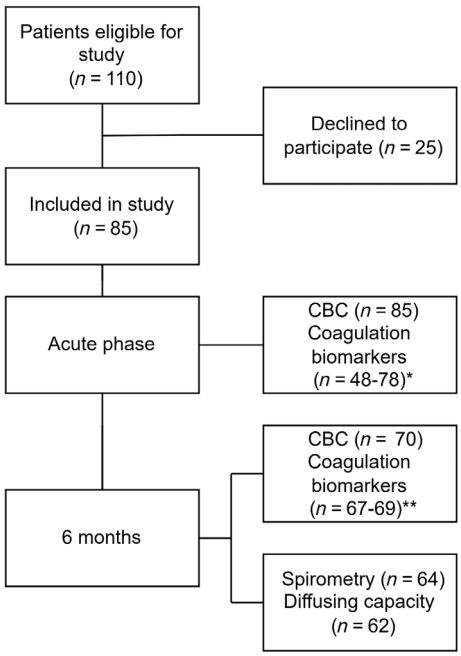

FIGURE 1 Flow chart of patient selection. *Different ICUs had varying protocols for ordering coagulation laboratory tests. **Samples for CBC and coagulation biomarkers were collected from patients consenting for research of the laboratory tests. CBC, complete blood count.

2.2.1 | CBC and coagulation biomarkers

The hospital laboratory analyzed the complete blood count (CBC) and coagulation biomarkers. CBC was analyzed from K2-EDTA tubes in a Sysmex® XN-9000 hematology analyzer (Kobe, Japan). Standardized coagulation assays in citrated (3.2%) plasma were performed in batches using ACL TOP® 500 and 750 analyzers (Instrumentation Laboratory, Naples, Italy) as follows: PT% with Owren's PT (Medirox®, Nyköping, Sweden), APTT, fibrinogen with Clauss method, one stage FVIII activity, and AT activity. All analysis was based on HaemosIL® reagents (Instrumentation Laboratory, Naples Italy), and D-dimer levels were obtained in FEU units (HaemosIL D dimer HS 500). PT% is inversely proportional to PT measured in seconds. We extracted the most deranged values for CBC and coagulation biomarkers during the ICU stay.

2.2.2 | Spirometry

Spirometry (Medikro) was performed in line with the ATS/ERS guidelines (ATS/ERS 2005) using software 4.8.0 (Medikro Co, Kuopio, Finland), and Kainu gender-specific reference values.[21] After the baseline measurements, patients inhaled 400 µg salbutamol via a spacer (Volumatic®, GSK, England), and the measurements were repeated 15 min later. We evaluated FVC, which is the maximal volume of air exhaled with a maximally forced effort from a maximal inspiration.[22] The spirometry values are presented by *z*-score, which expresses how many standard deviations a measured value is deviated from its predicted value.

2.2.3 | Diffusing capacity

Diffusing capacity (DLCO) was measured with a single-breath method (Jaeger Masterscreen-PFT, Sentry Suite software version 3.1, Vyaire Medical, Würzburg, Germany), using the gender-specific Viljanen references.[23,24] DLCO represents the lung capacity to transfer gas from inspired air to the bloodstream.[24] As the study variable, we recorded the hemoglobin-corrected diffusing capacity for carbon monoxide (DLCOc), utilizing the DLCOc percentage of the predicted value (DLCOc%). The result is reported as the mean of two measurements.

TABLE 1 Baseline characteristics of the 85 patients treated in intensive care units (ICU) due to a SARS-CoV-2 infection.

Sex	
Male, *n* (%)	52 (61)
Female, *n* (%)	33 (39)
Age, years, median (IQR)	60 (50–68)
BMI, kg/m^2, median (IQR)	30.1 (27.2–34.3)
Smoking	
Never, *n* (%)	56 (65)
Former, *n* (%)	29 (34)
Current, *n* (%)	0 (0)
One or more comorbidities, *n* (%)	67 (78)
Hypertension, *n* (%)	49 (58)
Dyslipidemia, *n* (%)	29 (34)
Type 1 diabetes, *n* (%)	2 (2)
Type 2 diabetes, *n* (%)	18 (21)
CAD or PAD, *n* (%)	12 (14)
Atrial fibrillation, *n* (%)	2 (2)
Previous DVT/PE or thrombophilia, *n* (%)	7 (8)
Chronic kidney failure, *n* (%)	3 (4)
Asthma, *n* (%)	13 (15)
COPD, *n* (%)	1 (1)
Obstructive sleep apnea, *n* (%)	14 (17)
Hypothyroidism, *n* (%)	5 (6)
Rheumatoid arthritis, *n* (%)	6 (7)
Gout, *n* (%)	5 (6)
Cancer, *n* (%)	2 (2)
Neurological disease[a], *n* (%)	2 (2)
Anticoagulant therapy preceding COVID-19[b], *n* (%)	6 (7)
Indications	
Atrial fibrillation, *n* (%)	2 (2)
Previous DVT/PE or thrombophilia, *n* (%)	4 (5)
Anticoagulant therapy at 6 months[c], *n* (%)	9 (11)
Indications	
Atrial fibrillation, *n* (%)	2 (2)
Previous DVT/PE or thrombophilia, *n* (%)	4 (5)
COVID-19 related pulmonary embolism, *n* (%)	3 (4)
Chest CT scan at 6 months[d], *n* (%)	16 (19)
Ground glass opacification, *n* (%)	12 (14)
Parenchymal bands, *n* (%)	8 (9)
Bronchus dilatation, *n* (%)	6 (7)
Reticular changes, *n* (%)	5 (6)
Traction bronchiectasis, *n* (%)	4 (5)
Fibrosis, *n* (%)	4 (5)
Acute pulmonary embolism, *n* (%)	0 (0)
Chronic thromboembolic pulmonary, *n* (%)	0 (0)

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; IQR, interquartile range; PAD, peripheral arterial occlusive disease; PE, pulmonary embolism.

[a]Patients with major neurological disease were excluded, but patients with stable epilepsy or migraine could be included.

[b]The specific anticoagulants used were warfarin in five patients and apixaban in one patient.

[c]The anticoagulant therapy was warfarin in seven patients, and apixaban in two patients.

[d]CT scan on clinical indication 4–7 months after hospital discharge.

TABLE 2 Characteristics of intensive care unit (ICU) treatment of the 85 patients admitted to ICU due to acute SARS-CoV-2 infection.

Time from symptom onset to ICU admission, days, median (IQR)	10 (8–13)
Invasive mechanical ventilation, *n* (%)	55 (65)
Duration of invasive mechanical ventilation, days, median (IQR)	12 (7–16)
Prone position, *n* (%)	27 (32)
Enoxaparin	
Prophylactic dose[a], *n* (%)	68 (80)
Therapeutic dose[b], *n* (%)	17 (20)

Abbreviations: ICU, intensive care unit; IQR, interquartile range.
[a]Enoxaparin at prophylactic dose <1.5 mg/kg/day.
[b]Enoxaparin at therapeutic dose >1.5 mg/kg/day.

2.3 | Statistical analysis

We report categorical variables as frequencies and percentages and continuous variables using median and interquartile range (IQR) for the non-parametric data. Continuous variables were compared over time with the related-samples Wilcoxon signed-rank test. We calculated delta (Δ) variables for each CBC and coagulation biomarker by subtracting the value at the acute phase from the one at 6 months. Correlations were assessed using the Pearson correlation for normally distributed data, and the Spearman correlation for non-normally distributed data. To account for multiple testing in the correlation analysis between coagulation biomarkers and lung function tests, we applied false discovery rate-correction (Benjamini–Hochberg Adjusted *p* value). We performed a linear regression analysis with diffusing capacity (DLCOc%) as the dependent variable. The regression model was adjusted for covariates (age, sex, and duration of invasive mechanical ventilation [IMV]), chosen based on their known associations with our dependent variable.[3,25,26] A *p*-value less than .05 was considered statistically significant. We disclosed the extent of missing data in the manuscript but did not perform imputation.

We performed statistical analysis using SPSS version 28 (IBM SPSS Statistics for Macintosh, IBM Corp., Armonk, NY, USA).

3 | RESULTS

The study population comprised 85 patients, with a median age of 60, 52 (61%) were male, and most were obese (the median BMI 30.1) Most patients had one or more comorbidities (Table 1). Two-thirds were treated with IMV, and one-third with a prone position at least once during acute COVID-19 (Table 2, Supplementary Table 2). The time between hospital discharge and the FU ranged from 122 to 235 days (median [IQR] 169 [162–177]).

The median values of most CBC and coagulation biomarkers, which were abnormal during the acute infection, were within the normal range when assessed individually (Figure 2B, Supplementary Table 3). However, only 21% of patients (15/70) had all CBC and coagulation activity biomarker levels fully normalized. The median values of hemoglobin levels and leukocyte counts normalized at 6 months, exhibiting a significant change compared to the acute phase (Figure 2). However, leukocyte count remained elevated in 26% (18/70) (Supplementary Table 3). The median values of fibrinogen, FVIII, and D-dimer levels were above the reference range during the acute phase of COVID-19 disease but decreased significantly by the 6-month FU (Figure 2B). However, FVIII levels remained elevated in 46% (31/68) and D-dimer in 27% (18/67) of patients (Supplementary Table 3). During the acute phase, both PT% and AT levels were within the low-normal range but displayed a significant increase at the 6-month FU, although the levels remained within the reference range (Figure 2B). No significant change was detected in APTT between the acute phase and 6-month FU (Figure 2B). The highest median value of C-reactive protein (CRP) during the acute phase (median (IQR)) was 246 (194–303) mg/L but normalized at 6-month FU (median (IQR)) 0 (0–0) mg/L.

Our previously published data regarding PFT is presented in Supplementary Table 4. In the correlation analysis between coagulation biomarkers and PFT at 6 months, we observed a negative correlation between diffusing capacity and FVIII, as presented in Figure 3 and Supplementary Table 5.

In multivariable analysis, with sex, age, and duration of IMV used as covariates, DLCOc% was associated with FVIII obtained at 6 months FU (Cohen's *d* 0.103, 95% CI −0.205 to −0.001, $p = .049$) (Supplementary Table 6). Between DLCOc% and any other included variable (age, sex, and duration of intubation), we found no statistically significant association.

We also assessed the correlations between coagulation biomarkers and DLCOc% at 6 months excluding patients who were on anticoagulation therapy at that time (Supplementary Table 7). In this analysis, the correlation between DLCOc% and FVIII no longer existed. However, we found a modest ($r = 0.41$) but statistically significant ($p = .020$) correlation between DLCOc% and AT (Supplementary Figure 1).

4 | DISCUSSION

In this observational follow-up study on patients previously treated in ICU for acute COVID-19, we assessed CBC and coagulation biomarkers at 6 months after hospital discharge, and their recovery from the acute phase, as well as the intercorrelations between coagulation biomarkers and lung function at 6 months. Our main findings indicated nearly normal CBC and coagulation biomarker levels regarding most variables at 6 months. However, only a small number of patients had all CBC and coagulation biomarker levels within the reference range. Markedly deranged coagulation biomarkers during the acute phase had almost entirely normalized. However, the elevation of FVIII levels persisted in half of the patients, leukocyte counts, and D-dimer in one-fourth of the patients. Considering the correlation between coagulation biomarkers and PFT at FU, we observed a weak negative correlation between DLCOc% and FVIII. In multivariable analysis, we

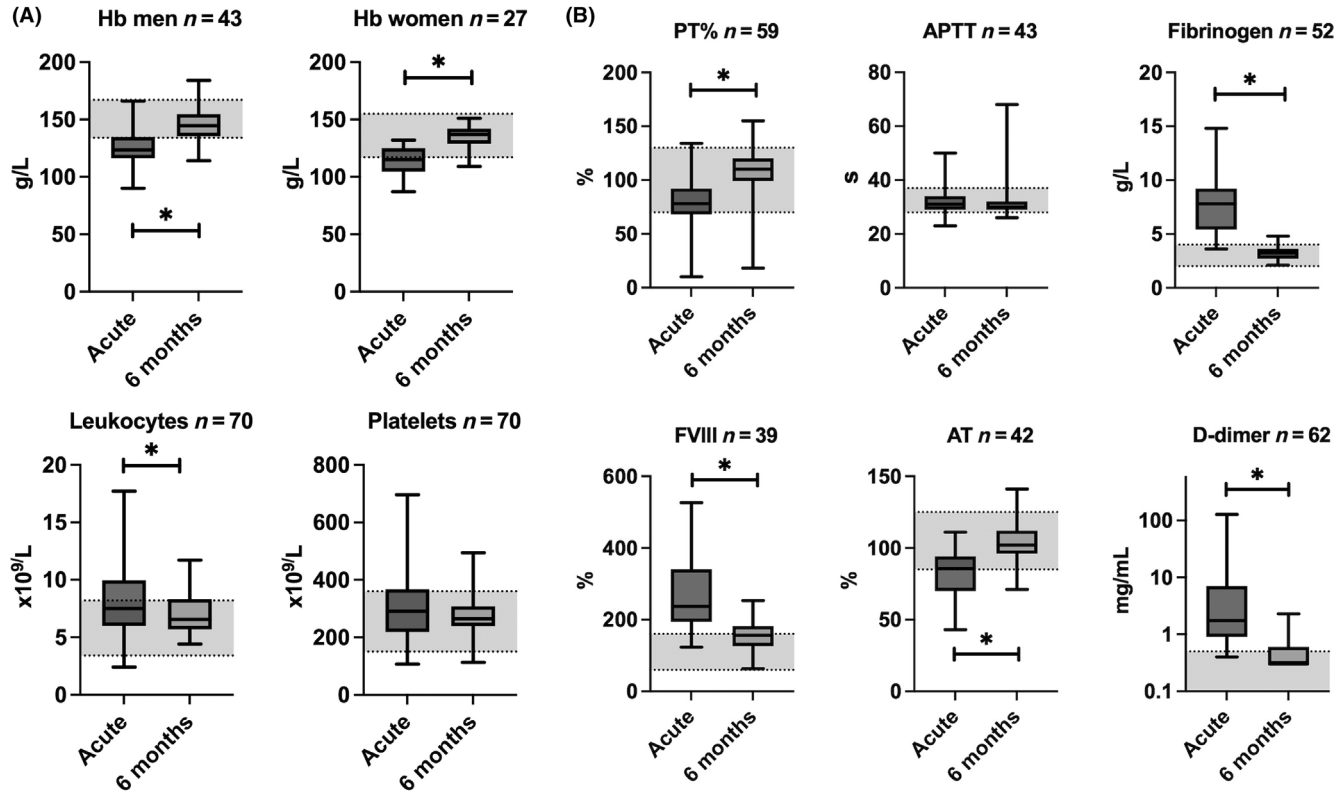

FIGURE 2 Comparison of complete blood count (A) and coagulation biomarkers (B) between the acute phase and 6 months after hospital discharge in 85 patients treated in intensive care unit for acute COVID-19. Boxes represent the interquartile ranges. Median is represented by the line that divides the box. Whiskers depict the lowest and highest values. Gray zone represents the reference range. D-dimer is presented in half logarithmic scale. *p < .001. 6 mo, 6-month follow-up; Acute, acute phase; APTT, activated partial thrombin time; AT, antithrombin; FVIII, coagulation factor VIII; Hb, hemoglobin; PT%, prothrombin time activity (%) (PT% is inversely proportional to PT measured in seconds).

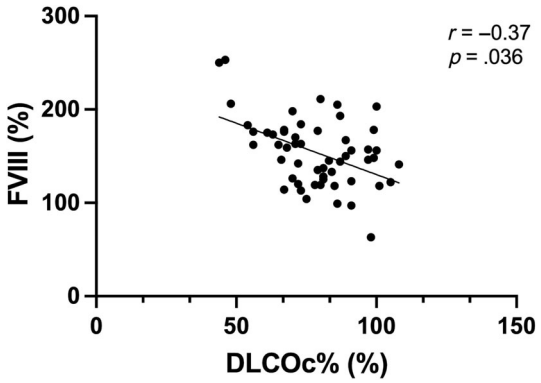

FIGURE 3 Correlation between diffusing capacity and FVIII 6 months after hospitalization for COVID-19 disease in 55 patients treated in intensive care units. DLCOc% represent DLCOc % of predicted, diffusing capacity for carbon monoxide corrected for hemoglobin. FVIII, coagulation factor VIII.

found an independent association between DLCOc% and FVIII, albeit with a small effect size. This supports our initial findings from the correlation analysis. However, the association was no longer significant when we excluded patients on anticoagulant therapy from the analysis.

During the acute phase, we found mild anemia, but the hemoglobin values normalized during the FU. Anemia is a common and often persistent finding among critically ill patients due to inflammation.[27-29] In the acute phase of COVID-19, anemia is related to critical COVID-19,[30] and aligned with other coagulation abnormalities.[31] Persistent anemia is also common in convalescent COVID-19 patients,[5] but was not found in our patients. Furthermore, the leukocyte count decreased at the 6-month FU but it remained abnormal in every fourth patient, consistent with a previous study.[32] In addition to anemia and leukocytosis, both thrombocytosis and mild thrombocytopenia are common during the acute phase of COVID-19.[28,31] Platelets are activated and adhere to pulmonary microvasculature, leading to coagulation activity, fibrin formation and impaired lung perfusion and function.[33] Persistently abnormal platelet counts were not evident in our data during a later phase of recovery.

Fibrinogen, FVIII, and D-dimer values were high and over the reference range during the acute phase but had normalized by 6 months in most patients. However, the median levels of FVIII remained at the upper level of the reference range. FVIII remained above the reference range in half of the patients, while D-dimer was above the reference range in every fourth patient. Fibrinogen is enzymatically converted by thrombin to engage in fibrin amyloid micro-clots, which are resistant to fibrinolysis and impair gas exchange.[8,34] This

phenomenon, accompanied by endothelial and platelet pathologies, is present in PASC patients.[8,34] Furthermore, fibrinogen binds to form fibrin amyloid micro-clots resulting in gas exchange disturbances in both the acute and recovery phases. We observed persistently elevated levels of fibrinogen in nine patients with no association with lung function test results. Our finding of FVIII is consistent with previous studies that reported elevated levels of FVIII in convalescent COVID-19 patients compared with controls.[29,30] Von Willebrand factor (VWF) carrying FVIII, an acute phase reactant, is released due to endothelial cell injury of pulmonary cells[35] and of vasculature overall. Additionally, elevated levels of plasma FVIII may reflect continued endothelial cell activity[29,30] and circulating microparticles.[36] According to Fogarty et al., endotheliopathy is independent of the acute phase response or NETosis but enhances thrombin generation post-COVID-19.[37] During acute COVID-19, an increased D-dimer value is the most typical net finding of the coagulopathy,[38] and prolonged elevation has been reported up to 4 months after initial infection.[14,16] Furthermore, in a previous study, low hemoglobin has been associated with high FVIII activity and D-dimer levels,[31] compatible with the procoagulant role of red blood cells.[39] Hypercoagulation in acute COVID-19 is driven by the interaction between thrombosis and inflammation.[10] Alongside coagulopathy, levels of fibrinogen, FVIII, and D-dimer can also increase due to inflammation in acute COVID-19.[31] Furthermore, inflammation during acute COVID-19 has been shown to induce lung injury, manifesting as impaired lung function during the recovery phase.[40] As inflammation biomarkers, we only considered CRP and leukocyte count. Elevated levels of leukocyte count, also observed in our patients during recovery, can indicate persistent inflammation,[41] although CRP was normalized in all patients during the same phase. Inflammation during the acute phase may explain most if not all of the observed association between coagulation and lung injury.

Our results from both univariable and multivariable analysis align with existing data suggesting that COVID-19 is characterized by endothelial injury and thromboembolism, which can lead to lung injury.[5,7] However, our study design does not allow assessing any causality between coagulation and lung function. Notably, the association between FVIII and DLCOc% lost significance when patients on anticoagulant therapy were excluded from the analysis. Interestingly, all six patients who were on anticoagulation therapy before COVID-19 were among the nine patients who received anticoagulant therapy at the 6-month FU. This may suggest that standard anticoagulation may not adequately address the inflammation induced by COVID-19.

We found an increase in PT% and AT levels, between the acute phase and 6-month FU. The median AT values were near the low-normal range during the acute phase. Levi et al. showed a mild prolongation in the PT in patients with severe COVID-19 during the initial infection,[38] which is in agreement with our results. Decreased PT% and AT levels reflect the enhanced thrombin generation and consumption related to critical illness.[42] However, nine patients in our dataset were receiving anticoagulation therapy at 6 months, which is a confounding factor when interpreting our PT% results. When patients on anticoagulation therapy were excluded, we observed a modest positive correlation between DLCOc% and AT. Bergantini et al. showed an inverse correlation between serum AT and PFT in patients with idiopathic pulmonary fibrosis (IPF) treated with nintedanib,[43] which is controversial to our findings. Several factors such as different patient characteristics and treatment approaches could explain this observation. In contrast to the findings of Bergantini et al., most patients in our study had normal AT levels at FU.[43] Furthermore, it is important to note that IPF and PASC are distinct disease entities.

Our study has limitations. We had a single-center design and focused on one diagnosis. Our sample size was small, and we did not perform an a priori power calculation. Exclusion of patients who did not have Finnish as their primary language and those with major neurological diagnoses may limit the generalizability of our results. We used clinical laboratory samples recorded during the acute phase, which led to incomplete availability of results of CBC and coagulation biomarkers, which may introduce selection bias. Baseline information regarding the potential premorbid coagulation abnormalities and lung function was not available. Additionally, we did not use a comparison group of patients with ARDS of other aethiology. Upon excluding the patients on anticoagulant therapy from the correlation analysis, we found a modest correlation between DLCOc% and AT and the correlation between DLCOc% and FVIII was no longer significant. Despite the severity of acute illness being a common denominator in the recovery of lung function and coagulation among convalescent COVID-19 patients, we chose not to include traditional intensive care mortality prediction scores in the linear regression analysis due to their limited suitability for COVID-19.[44] Additionally, our approach is a simplification when assuming linearity in coagulation parameters. We recognize that not all the studied parameters studied exhibit linear properties, which may have implications for the accuracy and generalizability of the results. Furthermore, inflammation that influences both coagulation and lung function could serve as an unmeasured common factor in the correlation analysis.

5 | CONCLUSION

In conclusion, most abnormal CBC and coagulation biomarker values normalized by the 6-month FU after critical COVID-19. However, only a small number of patients achieved full normalization of all values. A weak negative correlation between DLCOc% and FVIII suggests that coagulation plays a role in the prolonged lung tissue damage, but given the limitations of the study, the result is strictly hypothesis generating.

AUTHOR CONTRIBUTIONS

This study was designed by SK and JH. SK and HP analyzed the data, while SK, HP, JR, and JH interpreted the results. SK wrote the initial draft with assistance from HP, JR, and JH. All authors contributed to writing the manuscript and have read and approved the final version.

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DATA AVAILABILITY STATEMENT

Research data are not shared.

FUNDING INFORMATION

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ORCID

Salla Kattainen https://orcid.org/0000-0002-7380-1779

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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