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# POSTER ABSTRACTS

## 113.HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIA: BASIC AND TRANSLATIONAL

### Whole Blood Adhesion to VCAM-1 and P-Selectin and RBC Mechanical Fragility Can be Compromised in Long COVID-19 Patients with Sickle Cell Disease

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**Abstract** **Introduction:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause severe vascular complications associated with endothelial dysfunction and systemic inflammation. COVID19-specific IgG are detectable within a week of infection. Long COVID-19 has been described in patients continuing to exhibit symptoms after the virus is no longer detectable in the respiratory secretions, including fatigue, dyspnea, headache, and brain fog. The recent FAIR Health study reviewed a total of 1,959,982 COVID-19 patients for the prevalence of long COVID symptoms and reported that 23.2% had at least one post-COVID symptom [1]. The underlying biologic mechanisms of long COVID remain unclear, thus treatments are limited to symptomatic relief and supportive care. Many long COVID symptoms are consistent with systemic inflammation and impaired oxygen delivery observed in individuals with sickle cell disease (SCD), in turn associated with elevated blood cell adhesion and decreased red blood cell (RBC) stability. The aim of this study was to determine if deleterious changes in in blood cell properties related to adhesion and membrane stability under stress can be associated with the symptoms of long COVID-19. In this work we evaluated 7 SCD patients that were diagnosed with SARS-Cov-2 and tracked their recovery using semiquantitative IgG and blood cell function assays.

**Methods:** Blood samples were collected by the Foundation for Sickle Cell Disease (SCD) Research from SCD (homozygous SS, n=6) patients coming for regular or urgent clinic visit with SARS-CoV-2 serological and blood cell functions tests performed per the standard of care. Semiquantitative IgG assay was performed using DXi-80 (Beckman Coulter). Flow adhesion of whole blood to VCAM-1 (FA-WB-VCAM)and P-Selectin (FA-WB-Psel) substrates were determined by counting the cells that remain adherent in a microfluidics channel after perfusion with whole blood 1:1 diluted with HBSS buffer and washed by reversed flow at 1 dyne/cm $^2$. Red blood cell mechanical fragility (RBC MF) was measured as hemolysis induced by an oscillating cylindrical magnet with periodic non-invasive probing of cell-free hemoglobin fraction. Six individuals with SCD recovering from SARS-Cov-2 with biomarker data available both before and for more than 3 months after the infection (179±62 days) were included in the study.

**Results:** IgG levels varied from less than 0.1 to 37, with positive values being defined as IgG > 1. The median estimated half-life of IgG decline was 53 days ranging from 25 to 90 days (the last, for the hospitalized patient). Averaged for IgG positive (IgG+) and IgG negative (IgG-) conditions, combining pre- and post-infection IgG- conditions, values of patient hemoglobin (Hb), FA-WB-VCAM, FA-WB-Psel, and RBC MF cell properties lacked statistical significance (under both a paired t-test and population statistics). Hb levels remained essentially unchanged regardless of the time from infection or IgG status. However, FA-WB-VCAM, FA-WB-Psel, and RBC MF were all significantly elevated after SARS-Cov-2 seroconversion and remained elevated despite declining IgG levels (e.g., Fig. 1). These increases in biomarker values were statistically significant for both FA-WB-VCAM and RBC MF, and were approaching significance for FA-WB-Psel ($p<0065$). These increases were highly patient-specific with potential return to pe-infection values observed in some cases at about 5-6 months after the infection. A qualitative review of the medical records indicated a new subjective report of fatigue in 5 of 6 patients. Longer observations are required to determine if abnormal blood cell adhesive properties and RBC membrane instability are mechanisms of long-COVID-19 pathophysiology.

**Conclusions:** Whole blood adhesion to both p-selectin and VCAM-1 as well as RBC membrane stability can be significantly impaired in convalescent SARS-Cov-2 patients suggesting an association with long COVID-19. New and emerging treatments

that modify whole blood adhesive properties and RBC membrane stability should be investigated for their potential to accelerated recovery from long COVID-19.
Health F. A Detailed Study of Patients with Long-Haul COVID: An Analysis of Private Healthcare Claims; White Paper. June 15, 2021

**Disclosures Tarasev:** *Functional Fluidics:* Current holder of *stock options* in a privately-held company. **Ferranti:** *Functional Fluidics:* Current holder of *stock options* in a privately-held company. **Allen:** *Functional Fluidics:* Current Employment. **Gao:** *Functional Fluidics:* Current Employment. **Topping:** *Functional Fluidics:* Current Employment. **Ferranti:** *Functional Fluidics:* Current Employment. **Makinde-Odesola:** *Functional Fluidics:* Other: conduct research for academic program. **Hines:** *Functional Fluidics:* Current holder of *stock options* in a privately-held company.

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