Microvascular Remodeling and Endothelial Dysfunction Across the Post-COVID-19 Spectrum: A Prospective Observational Case-Control Study

Timon Wallraven[1], Roman Günthner[1], Isabelle Lethen[1], Andrea Ribeiro[1], Maciej Lech[2], Frederike Cosima Oertel[3,4,5], Lukas G. Reeß[3], Bernhard Haller[6], Lukas Streese[7,8], Henner Hanssen[9], Michael Wunderle[1*] & Christoph Schmaderer[1,10*]

[1]TUM School of Medicine and Health, Department of Nephrology, TUM University Hospital, Technical University of Munich, Munich, Germany

[2]Medical Clinic and Polyclinic IV, LMU University Hospital Munich, Munich, Germany

[3]Experimental and Clinical Research Center, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, and Max Delbrück Center for Molecular Medicine, Germany

[4]Einstein Center Digital Future Berlin, Berlin, Germany

[5]Department of Neurology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, and Max Delbrück Center for Molecular Medicine, Germany

[6]TUM School of Medicine and Health, Institute for AI and Informatics in Medicine, TUM University Hospital, Technical University of Munich, Munich, Germany

[7]Faculty of Health Care, Therapeutic Sciences, Niederrhein University of Applied Sciences, Krefeld, Germany

[8]Department of Nephrology, Medical Faculty, University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

[9]Department of Sport, Exercise and Health, Preventive Sports Medicine and Systems Physiology, University of Basel, Basel, Switzerland

[10]German Centre for Infection Research (DZIF), Partner Site Munich, Munich, Germany

*Authors share senior authorship

Corresponding authors:
T. Wallraven; C. Schmaderer

Dependent variable ME/CFS			
Predictors	*Odds Ratios*	*CI*	*p*
Transferrin	0.99	0.97 – 1.00	**0.007****
IL 6	1.16	1.05 – 1.36	**0.018***
Creatinikinase	1.00	0.99 – 1.00	0.429
AVR	0.00	0.00 – 0.01	**0.001****
Neutrophile	1.06	1.02 – 1.12	**0.009****
ICAM-1	1.00	1.00 – 1.00	**0.040***
Observations	173		
R^2 Tjur	0.23		

Supplementary Table 1 Multivariable logistic regression with ME/CFS status as the dependent variable. Results are shown as odds ratios (OR) with 95% confidence intervals (CI) and p-values. The model included arteriolar–venular ratio (AVR), interleukin-6 (IL-6), neutrophil percentage, creatine kinase (CK), intercellular adhesion molecule-1 (ICAM-1) and transferrin. Model fit is summarized by Tjur's R^2. Statistical significance is indicated as: *p < 0.05; **p < 0.01; ***p < 0.001.

Data & Code Availability

Description	**Source/Repository**	**Persistent ID / URL**
Study registration (All Eyes on PCS Study)	ClinicalTrials.gov	ClinicalTrials.gov: NCT05635552
Study registration (Citrate–Acetate Study)	ClinicalTrials.gov	ClinicalTrials.gov: NCT05635552
Study registration (COMPLETE Study)	ClinicalTrials.gov	ClinicalTrials.gov: NCT02745340
Data availability	Available from corresponding author on reasonable request	Not publicly available (legal restrictions)
Code availability	Available from corresponding author on reasonable request	

Other

Description	**Source / Repository**	**Persistent ID / URL**
Dynamic Vessel Analyzer (DVA)	Imedos Health GmbH (Jena, Germany)	DVAlight
Static Vessel Analyzer (SVA)	Imedos Health GmbH (Jena, Germany)	VesselMap
Retinal camera	Topcon (Tokyo, Japan)	TRC-NW8
Cytometric Bead Array platform	BD Biosciences (San Diego, CA, USA)	CBA Flex System
Biomarker measurements	BD Biosciences	CBA Flex Sets: IL-6, ICAM-1, VCAM-1, MCP-1, CCL-5, CXCL10, VEGF
Statistical software	R Foundation for Statistical Computing	R version 4.2.1
Affinity publisher		Version 2.5.5

R packages used	CRAN	MatchIt; WeightIt; survey; gtsummary; ggplot2; pROC; corrplot

Supplementary Table 2 Major Resources Table

vFID as dependent variable

Predictors	*Estimates*	*CI*	*p*
PCS	-0.70	-1.42 – 0.01	0.054
gender [male]	-0.41	-1.25 – 0.43	0.34
Post-COVID-19 Syndrome × gender [male]	-0.23	-1.70 – 1.23	0.75
Observations	287		
R^2 / R^2 adjusted	0.026 / 0.016		

CRAE as dependent variable

Predictors	*Estimates*	*CI*	*p*
PCS	-7.13	-11.78 – -2.48	**0.003****
gender [male]	-4.51	-9.92 – 0.90	0.10
Post-COVID-19 Syndrome × gender [male]	3.09	-6.22 – 12.41	0.51
Observations	296		
R^2 / R^2 adjusted	0.041 / 0.031		

AVR as the dependent variable

Predictors	*Estimates*	*CI*	*p*
PCS	-0.03	-0.05 – -0.01	**<0.001*****
gender [male]	0.00	-0.02 – 0.02	0.92
Post-COVID-19 Syndrome × gender [male]	0.01	-0.02 – 0.05	0.54
Observations	296		
R^2 / R^2 adjusted	0.049 / 0.039		

Supplementary Table 3 Linear regression models examining the associations between Post-COVID-19 syndrome (PCS) and DVA parameter vFID and SVA parameters (CRAE and AVR). Models included sex (male vs female) and a PCS × sex interaction term to test for sex-specific effects. Estimates represent unstandardized regression coefficients with 95% confidence intervals (CI). Statistical significance is indicated as: *p < 0.05; **p < 0.01; ***p < 0.001.

Baseline characteristics	**NI** n = 96	**Recovered** n = 102	**Post-COVID-19 Syndrome** n = 102	**p-value**
Age, years, mean (±SD)	43.0 (± 14.5)	33.3 (±11.4)	41.9 (±11.6)	**<0.001*****

Gender, female, n(%)	73 (76%)	73 (72%)	77 (75%)	>0.9
BMI, kg/m^2, mean (±SD)	23.2 (±3.7)	23.5 (±4.0)	24.5 (±4.8)	0.090
RR_{syst}[1],(mmHg), mean (±SD)	122.7 (±16.0)	116.7 (±15.7)	121.8 (±16.9)	**0.026***
Cardiovascular Risk Factors				
Arterial Hypertension, n(%)	0 (0%)	5 (4.9%)	16 (16%)	**<0.001****
Hypercholesterolemia, n(%)	-	6 (5.9%)	22 (22%)	**0.003***
Nicotine abuse, n(%)	11(11%)	14 (14%)	10 (9.8%)	0.7
Diabetes mellitus, n(%)	0 (0%)	0 (0%)	1 (1.0%)	0.4
Acute SARS-CoV-2 infection				
Number of infections, n(%)				**<0.001****
0	96 (100%)	0 (0%)	0 (0%)	
1	0 (0%)	62 (61%)	71 (70%)	
2	0 (0%)	31 (30%)	29 (28%)	
3	0 (0%)	8 (7.8%)	1 (1.0%)	
4	0 (0%)	1 (1.0%)	1 (1.0%)	
Severity of acute infection, n(%) (WHO progression scale)				**<0.001****
0	-	1(1.0%)	0 (0%)	
1	-	9(8.8%)	1 (1.0%)	
2	-	81(79%)	61(60%)	
3	-	10(9.8%)	34(33%)	
4	-	0 (0%)	4 (3.9%)	
5	-	0 (0%)	1 (1.0%)	
6	-	0 (0%)	1 (1.0%)	

8	-	1 (1.0%)	0 (0%)	
SARS-CoV-2 variants, n(%)				**0.004****
alpha	-	1 (1.0%)	7 (6.9%)	
delta	-	2 (2.0%)	13 (13%)	
omicron	-	20 (20%)	19 (19%)	
unknown	-	79 (77%)	63 (62%)	
PCS-related characteristics				
Duration of PCS, days, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	404.0 (291.0, 575.0)	-
Cumulatitive sick days, median (IQR)	-	0.0 (0.0, 0.0)	199.5 (44.0, 377.0)	**<0.001*****
Work loss during PCS, n(%)	-	0 (0%)	16 (16%)	**<0.001*****
PCS Severity Score, mean (±SD)	-	1.8 (5.9)	36.9 (10.6)	**<0.001*****
C19-YRS, mean (±SD)	-	-	32.4 (14.0)	-
GAD7, median (IQR)	-	-	5.0 (2.0, 9.0)	-
PHQ9, mean (±SD)	-	-	10.4(4.3)	-
FSS, median (IQR)	-	2.3 (1.6, 3.1)	6.1 (5.1, 6.7)	**<0.001*****
EQ5DL-Index, median (IQR)	-	-	0.6 (0.3, 0.8)	-
ME/CFS, n(%)	-	0 (0%)	62 (61%)	-
Comorbidities				
Depression, n(%)	-	10 (9.8%)	19 (19%)	0.2
Pre-existing mental conditions , n(%)	-	4 (4.0%)	8 (7.9%)	0.4
Laboratory values				

Leukocytes (G/L), mean (±SD)	6.0 (±1.5)	6.5 (±1.8)	6.7 (±1.8)	0.063
Platelets (G/L), mean (±SD)	-	270.5 (±56.7)	288.4 (±63.0)	**0.040***
Neutrophils (%), mean (±SD)	-	58.2 (±9.4)	62.5 (±8.4)	**0.001****
Lymphocytes (%), mean (±SD)	-	30.5 (±9.0)	28.0 (±7.7)	**0.041***
Monocytes (%), median (IQR)	-	7.5 (6.0, 9.0)	7.0 (6.0, 8.0)	0.071
Eosinophils (%), median (IQR)	-	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	**0.028***
Total Cholesterol (mg/dL), mean (SD)	195.9 (±35.2)	182.4 (±36.0)	202.9 (±44.3)	**0.002****
LDL (mg/dL), mean (±SD)	108.2 (±25.1)	107.3 (±34.4)	127.7 (±40.0)	**0.001*****
HDL (mg/dL), mean (±SD)	69.2 (±14.8)	62.6 (±15.3)	62.2 (±15.1)	0.057
Hemoglobin (g/dL), mean (±SD)	14.5 (±1.5)	13.4 (±1.6)	13.8 (±1.3)	**<0.001*****
Hematocrit (%),mean (±SD)	-	39.8 (±3.2)	40.4 (±3.2)	0.2
Ferritin (µg/L), median (IQR)	-	58.5 (27.5, 106.0)	78.0 (50.0, 152.0)	**0.008****
CRP(mg/dl), median (IQR)	0.016 (0.02, 0.09)	0.18 (0.10, 0.20)	0.22 (0.09, 0.20)	**<0.001*****
Transferrin (mg/dL), mean (±SD)	-	286.0 (±46.2)	260.9 (±33.2)	**<0.001*****
Transferrin Saturation (%),mean (±SD)	-	27.8 (±12.6)	27.8 (±10.9)	>0.9
RDW-CV (%), median (IQR)	-	12.6 (12.2, 13.2)	12.6 (12.1, 13.1)	0.3
MCHC (g/dL), mean (±SD)	-	34.0 (±1.2)	34.1 (±1.0)	0.5

D-Dimer (ng/mL), median (IQR)	-	237.0 (199.0, 330.0)	227.0 (199.0, 387.0)	0.7
aPTT (sec), mean (±SD)	-	29.4 (±3.2)	29.8 (±3.1)	0.4
LDH (U/L), mean (±SD)	-	177.4 (±30.7)	176.0 (±28.9)	0.7
Creatine Kinase (U/L), median (IQR)	-	110.0 (75.0, 154.0)	81.5 (58.0, 102.0)	**<0.001*** **
Total IgG (mg/dL), mean (±SD)	-	1,118.7 (±265.5)	1,081.1 (±204.4)	0.3
IgG1 (mg/dL), mean (±SD)	-	691.7 (±176.1)	669.5 (±137.3)	0.3
IgG2 (mg/dL), mean (±SD)	-	354.8 (±135.6)	357.4 (±113.8)	0.9
IgG3 (mg/dL), median (IQR)	-	31.0 (23.5, 40.4)	27.4 (19.5, 37.7)	**0.021***
IgG4 (mg/dL), median (IQR)	-	55.8 (33.2, 82.2)	47.2 (25.9, 80.2)	0.4
TSH (mIU/L), median (IQR)	-	1.6 (1.2, 2.1)	1.4 (1.0, 2.0)	0.2

Suplementary Table 4 presents baseline demographic, clinical, and laboratory characteristics of the three study cohorts: Never infected (NI) controls, Recovered individuals, and patients with Post-COVID-19 Syndrome (PCS). Continuous variables are reported as mean (±SD) or median (Q1, Q3), depending on distribution, and categorical variables as n (%). Statistical comparisons across groups were performed using one-way ANOVA, the Kruskal–Wallis test, or Pearson's χ^2 test, as appropriate. Abbreviations: Never infected, NI; BMI, Body Mass Index; RRsyst, Blood presure before RVA[1]; C19-YRS, COVID-19 Yorkshire Rehabilitation Scale; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; FSS, Fatigue Severity Scale; EQ-5D-5L, EuroQol 5-Dimension 5-Level index; ME/CFS, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; LDL, Low-Density Lipoprotein Cholesterol; HDL, High-Density Lipoprotein Cholesterol; LDH, Lactate Dehydrogenase; MCHC, Mean Corpuscular Hemoglobin Concentration; RDW-CV, Red Cell Distribution Width–Coefficient of Variation; TSH, Thyroid-Stimulating Hormone; aPTT, Activated Partial Thromboplastin Time; CK, Creatine Kinase; IgG, Immunoglobulin G; IgG1–4, Immunoglobulin G subclasses 1-4. Missing data are reported as number of missing observations (n) for each group in the following order: NI, recovered, and PCS. Missing values were as follows: systolic blood pressure before RVA (RRsyst ; 2, 11, 7); hypercholesterolemia (90, 0, 0); work loss during PCS (96, 0, 2); PCS Severity Score (90, 3, 0); C19-YRS score (96, 102, 1); PHQ-9 and GAD-7 (96, 102, 2); Fatigue Severity Scale (96, 5, 1); EQ-5D-5L index (96, 102, 57); ME/CFS status (-, 0, 1); depression diagnosis (96, 0, 0); pre-existing mental conditions (96, 1, 1); leukocytes (50, 8, 4); CRP (62, 7, 3); neutrophils (96, 12, 7); lymphocytes (96, 8, 4); monocytes (96, 8, 4); eosinophils (96, 10, 4); total cholesterol (62, 7, 3); LDL cholesterol (62, 19, 22); HDL cholesterol (62, 19, 22); hemoglobin (52, 7, 4); hematocrit, MCHC, RDW-CV, and platelets (all 96, 7, 4); D-dimer (96, 7, 13); aPTT (96, 7, 15); creatine kinase (96, 11, 4); ferritin (96, 6, 5);

transferrin (96, 6, 5); transferrin saturation (96, 6, 6); total IgG (96, 9, 3); IgG subclasses 1-4 (96, 9, 3); and TSH (96, 5, 3). Statistical significance is displayed as: * p < 0.05; ** p < 0.01;*** p < 0.001.

Laboratory value	**Comparison**	**Estimate (β)**	**95% CI**	**Standardized ß**	**p**
Hemoglobin (g/dL)	**NI vs. PCS**	0.75	0.26 – 1.25	0.20	**0.004****
	Recovered vs PCS	-0.34	-0.75 – 0.07	-0.12	0.103
CRP (mg/L)	**NI vs. PCS**	1.04	0.76 – 1.93	-0.41	**<0.001*****
	Recovered vs PCS	-0.05	-0.46 – 0.38	-0.02	0.682
Leukocytes (G/L)	**NI vs. PCS**	-0.69	-1.30 – -0.07	-0.14	**0.028***
	Recovered vs PCS	-0.24	-0.74 – 0.25	-0.07	0.335

Supplementary Table 5 Associations between cohort status and hemoglobin, C-reactive protein (CRP), and leukocyte counts estimated using linear regression models including NI, recovered, and PCS participants after correcting for age. PCS served as the reference category. Estimates represent beta coefficients with 95% confidence intervals. *p < 0.05; **p < 0.01; ***p < 0.001.

Laboratory value	**Mean difference**	**95% CI**	**p**
Neutrophils (%)	3.97	1.05 – 6.90	**0.008****
Lymphocytes (%)	-2.05	- 4.66 – 0.55	0.122
Platelets (G/L)	16.58	- 2.52 – 35.69	0.088
Ferritin (µg/L)	0.06	-	0.151
Transferrin (mg/dL)	-16.57	- 27.90 – - 5.24	**0.004****
LDL cholesterol (mg/dL)	10.10	- 2.32 – 22.52	0.110
Total cholesterol (mg/dL)	7.65	- 4.31 – 19.60	0.209
IgG3 (mg/dL)	-0.06	-	0.216
Creatine kinase (U/L)	-0.22	-	**<0.001*****

Suplementary Table 6 Group differences in laboratory values between PCS and recovered individuals were re-estimated in an age-balanced pseudo-population (ATO) using survey-weighted tests. Survey-weighted t-tests were applied for approximately normally distributed variables, and design-based rank tests were used for non-normally distributed variables (ferritin, IgG3, creatine kinase). Negative values indicate lower values in PCS than in recovered individuals **p < 0.01; *** p<0.001.

Dependent variable vFID						
	Estimate	**CI**	**p**	**Estimate (Std. ß)**	**CI**	**p**
NI	0.39	-0.33 – 1.11	0.291	0.37 (0.07*)	-0.36 – 1.11	0.319
Recovered	1.16	0.43 – 1.89	**0.002****	1.39 (0.25*)	0.62 – 2.15	**<0.001*****
Age				0.04	0.01 – 0.06	**0.002****
Art. Hypertension				-0.74	-2.0 – 0.5	0.204
BMI				0.07	-0.01 – 0.2	0.055
RR_{syst}				-0.01	-0.03 – 0.01	0.256
Observations	295			271		
R^2 / R^2 adjusted	0.05 / 0.04			0.08 / 0.06		

Dependent variable CRAE

	Estimate	CI	p	Estimate (Std. ß)	CI	p
NI	5.83	1.49 – 10.17	**0.009****	5.01 (0.15*)	0.76 – 9.26	**0.021***
Recovered	7.82	3.54 – 12.11	**<0.001*****	3.52 (0.11*)	-0.74 – 7.78	0.105
Age				-0.33	-0.48 – -0.19	**<0.001*****
Art. Hypertension				-5.59	-12.7 – 1.5	0.123
BMI				0.05	-0.39 – 0.48	0.834
RR_{syst}				-0.21	-0.32 – -0.10	**<0.001*****
Observations	295			275		
R^2 / R^2 adjusted	0.05 / 0.04			0.21 / 0.19		

Dependent variable CRVE						
	Estimate	**CI**	**p**	**Estimate**	**CI**	**p**
NI	-1.7	-6.2– 2.9	0.45	-1.25	-5.96 – 3.45	0.601
Recovered	4.1	-0.4 – 8.6	0.08	0.46	-4.35 – 5.26	0.852
Age				-0.30	-0.46 – -0.14	**<0.001*****
Art. Hypertension				-5.14	-12.9 – 2.65	0.195
BMI				0.57	0.09 – 1.05	**0.021***
RR_{syst}				-0.11	-0.24 – -0.01	0.066
Observations	295			275		
R^2 / R^2 adjusted	0.02 / 0.02			0.1 / 0.09		

Dependent variable AVR						
	Estimate	**CI**	**p**	**Estimate (Std. ß)**	**CI**	**p**
NI	0.04	0.02 – 0.05	**<0.001*****	0.03 (0.21*)	0.01 – 0.05	**0.002****
Recovered	0.02	0.00 – 0.04	**0.017***	0.01 (0.10*)	-0.01 – 0.03	0.167
Age				-0.0	-0.00 – 0.00	0.241
Art. Hypertension				-0.01	-0.04 – 0.02	0.521
BMI				-0.00	-0.00 – 0.00	0.057
RR_{syst}				-0.00	-0.00 – 0.00	**0.041***
Observations	295			275		
R^2 / R^2adjusted	0.05 / 0.04			0.10 / 0.08		

Supplementary Table 7 Multivariable linear regression models assessing associations between cohort status (NI and recovered, each compared with the reference group PCS) and RVA parameters, including vFID, CRAE, CRVE and AVR. Unadjusted models are shown in left columns. Adjusted models (right columns) additionally include age, sex, arterial hypertension, body mass index (BMI), and systolic blood pressure prior to retinal vessel analysis (RRsyst). Estimates are presented as regression coefficients with 95% confidence intervals (CI). *Standardized (Std.) ß-coefficients are presented in brackets. Sample sizes vary across models due to missing covariate data. Model fit is summarized using R^2 and adjusted R^2. PCS served as the reference category in all models. Significance levels are indicated as *$p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.

Variable	Mean Difference	95% CI	p-value
AVR	-0.02	-0.04 - 0.0003	0.053

CRAE(µm)	-5.6	-10.3 - -0.8	**0.022***
CRVE(µm)	-2.2	-7.0 - 2.6	0.36
vFID(%)	-1.3	-2.0- -0.5	**0.0012****
aFID(%)	-0.4	-1.1 - 0.2	0.19

Supplementary Table 8 Sensitivity analysis adjusting for age using overlap weighting (ATO). Group differences in RVA parameters were re-estimated using survey-weighted t-tests in an age-balanced pseudo-population. Negative values indicate lower values in PCS than in recovered individuals. *p < 0.05; **p < 0.01.

Post-hoc Tukey HSD comparisons for AVR between cohorts

Comparison	*Adjusted p-value (post-hoc)*
PCS with ME/CFS vs. NI	**<0.001*** **
PCS without ME/CFS vs. NI	0.328
Recovered vs. NI	0.274
PCS without ME/CFS vs. PCS with ME/CFS	0.131
Recovered vs. PCS with ME/CFS	**0.010****
Recovered vs. PCS without ME/CFS	0.987

Post-hoc Tukey HSD comparisons for CRAE between cohorts

Comparison	*Adjusted p-value (post-hoc)*
PCS with ME/CFS vs. NI	0.263
PCS without ME/CFS vs. NI	0.433
Recovered vs. NI	0.624
PCS without ME/CFS vs. PCS with ME/CFS	1.00
Recovered vs. PCS with ME/CFS	**0.020***
Recovered vs. PCS without ME/CFS	0.073

Post-hoc Tukey HSD comparisons for vFID between cohorts

Comparison	*Adjusted p-value (post-hoc)*
PCS with ME/CFS vs. NI	0.890
PCS without ME/CFS vs. NI	0.790
Recovered vs. NI	0.140
PCS without ME/CFS vs. PCS with ME/CFS	0.991
Recovered vs. PCS with ME/CFS	**0.046***
Recovered vs. PCS without ME/CFS	0.052

Supplementary Table 9 Post-hoc pairwise comparisons for RVA parameters vFID, CRAE and AVR, central between never infected (NI) controls, recovered individuals, PCS patients without ME/CFS, and PCS patients fulfilling ME/CFS criteria. Comparisons were performed following overall group differences using one-way analysis of variance with Tukey's honestly significant difference (HSD) correction for multiple testing. Adjusted p-values are reported. Statistical significance is indicated as *p < 0.05, **p < 0.01, and *** p < 0.001.

	vFID as the dependent variable		
Predictors	*Estimates (Std. ß)*	*CI*	*p*
NI	0.20 (0.03*)	-0.65 – 1.05	0.642
PCS without ME/CFS	-0.33 (-0.04*)	-1.36 – 0.70	0.519
Recovered	1.26 (0.23*)	0.41 – 2.11	**0.004****
Age	0.04	0.01 – 0.06	**0.004****
Gender [male]	-0.38	-1.11 – 0.36	0.314
BMI	0.07	-0.01 – 0.15	0.076
RR_{syst}[1]	-0.01	-0.03 – 0.01	0.466
Arterial hypertension	-0.77	-2.00 – 0.45	0.217

	CRAE as the dependet variable		
Predictors	*Estimates (Std. ß)*	*CI*	*p*
NI	5.03 (0.14*)	-0.44 – 10.50	0.063
PCS without ME/CFS	1.78 (0.03*)	-4.88 – 8.43	0.611
Recovered	3.88 (0.11*)	-1.57 – 9.32	0.156
Age	-0.34	-0.50 – -0.17	**<0.001*** **
Gender [male]	-1.21	-5.93 – 3.51	0.601
BMI	0.05	-0.44 – 0.54	0.812
RR_{syst}[1]	-0.22	-0.36 – -0.09	**0.001** **
Arterial hypertension	-5.19	-13.09 – 2.71	0.185

	AVR as the dependent variable		
Predictors	*Estimates (Std. ß)*	*CI*	*p*
NI	0.04 (0.32*)	0.02 – 0.07	**<0.001*** **
PCS without ME/CFS	0.03 (0.14*)	0.00 – 0.05	**0.049***
Recovered	0.02 (0.17*)	0.00 – 0.05	**0.028***
Age	-0.00	-0.00 – 0.00	0.422
Gender [male]	0.01	-0.00 – 0.03	0.130
BMI	-0.00	-0.00 – 0.00	0.085
RR_{syst}[1]	-0.00	-0.00 – -0.00	**0.018***
Arterial hypertension	-0.01	-0.04 – 0.02	0.513

Supplementary Table 10 Multivariable regression analyses examining associations between cohort subgroups never-infected (NI), recovered individuals, and PCS patients without ME/CFS and RVA parameters vFID, CRAE and AVR. All models were adjusted for age, sex, body mass index (BMI), systolic blood pressure prior to retinal vessel analysis (RRsyst), and arterial hypertension. Regression coefficients are presented with 95% confidence intervals (CI) and corresponding p-values. *Standardized (Std.) ß-coefficients are presented in brackets. The reference group is PCS patients fulfilling ME/CFS criteria. Statistical significance is indicated as *p < 0.05, **p < 0.01, and *** p < 0.001.

Variable	**OR (95% CI)**	**p-value**	**AUC (95% CI)**	**Biological domain**
Creatine kinase	0.996 (0.99–1.00)	0.12	0.72 (0.64–0.80)	Muscle metabolism
IL-6	1.26 (1.10–1.51)	**0.005****	0.70 (0.61–0.78)	Inflammation
CRP	1.29 (0.46–3.38)	0.59	0.66 (0.56–0.76)	Inflammation
VCAM-1	1.00006 (1.00–1.00)	**0.027***	0.65 (0.57–0.74)	Endothelial activation
ICAM-1	1.0009 (1.00–1.00)	**0.002****	0.65 (0.56–0.73)	Endothelial activation
AVR	0.006 (0.000004–0.07)	**0.003****	0.62 (0.54–0.70)	Retinal microcirculation

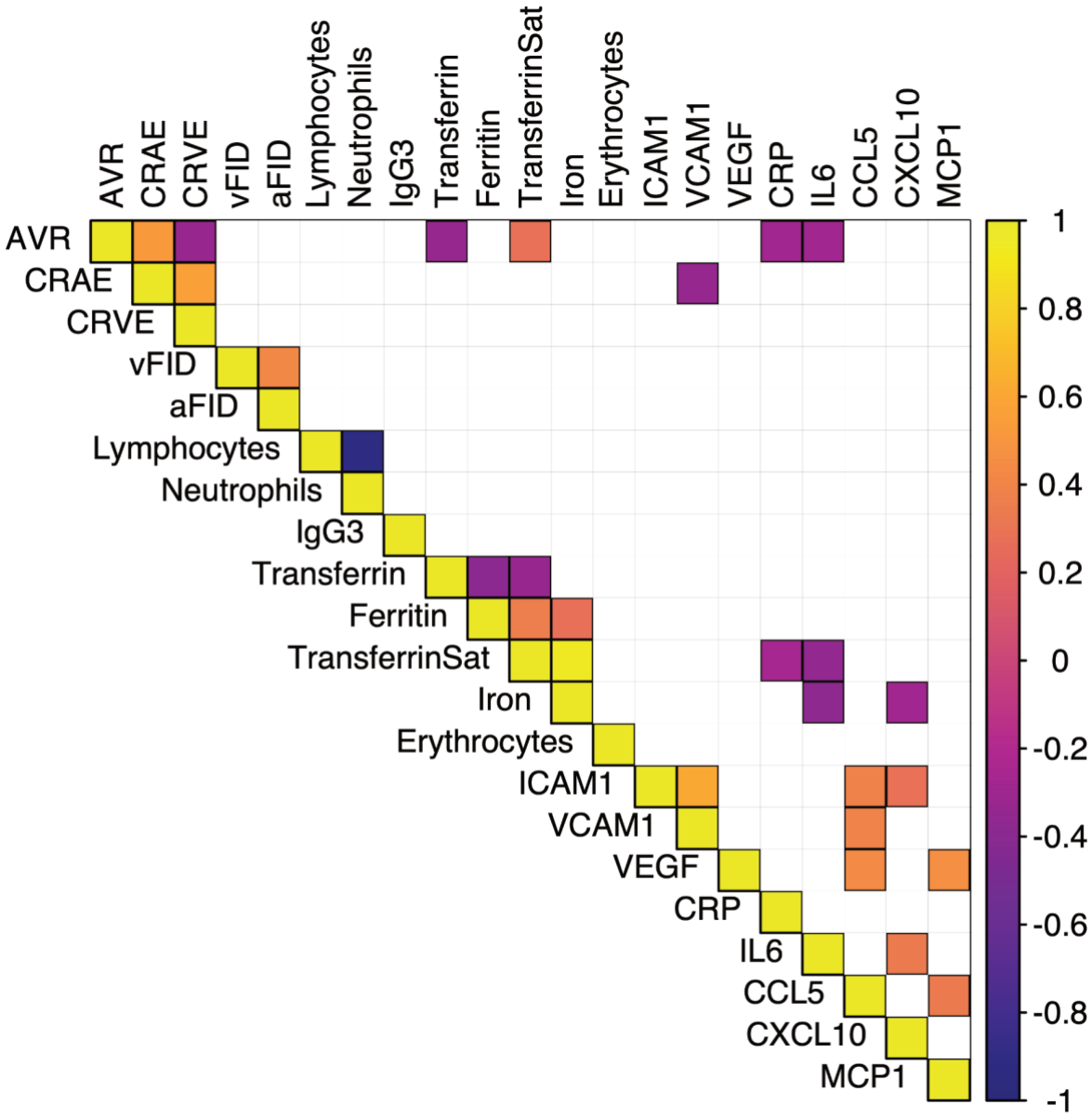
LDL cholesterol	1.01 (1.00–1.02)	**0.024***	0.62 (0.52–0.71)	Lipid metabolism
Transferrin	0.99 (0.98–1.00)	**0.008****	0.61 (0.53–0.69)	Iron metabolism
Cholesterol	1.01 (1.00–1.02)	**0.011***	0.61 (0.52–0.69)	Lipid metabolism
Platelets	1.01 (1.00–1.01)	**0.009****	0.61 (0.52–0.69)	Coagulation
Neutrophils	1.05 (1.01–1.09)	**0.012***	0.60 (0.53–0.69)	Inflammation
CRAE	0.98 (0.96–1.00)	**0.019***	0.60 (0.52–0.68)	Retinal microcirculation
aFID	0.87 (0.75–1.00)	0.063	0.60 (0.51–0.69)	Retinal microcirculation
vFID	0.90 (0.80–1.02)	0.10	0.58 (0.50–0.66)	Retinal microcirculation
Ferritin	1.00 (1.00–1.00)	0.59	0.57 (0.49–0.66)	Iron metabolism
MCP-1	1.01(0.99 - 1.03)	0.070	0.57 (0.49-0.66)	Inflammation
aPTT	1.03 (0.93–1.14)	0.52	0.55 (0.46–0.64)	Cogualtion
IgG3	0.99 (0.97–1.01)	0.49	0.54 (0.46–0.63)	Humoral immunity
IgG	1.00 (1.00–1.00)	0.49	0.54 (0.46–0.63)	Humoral immunity
CCL-5	1.00 (1.00–1.00)	0.20	0.54 (0.45–0.63)	Inflammation
TAG	1.00 (1.00–1.01)	0.64	0.53 (0.44–0.63)	Lipid metabolism
Hemoglobin	1.13 (0.91–1.42)	0.30	0.53 (0.44–0.62)	Oxygen transport
Prothrombin time	1.00 (NA–1.00)	0.64	0.53 (0.43–0.62)	Coagulation
CRVE	1.00 (0.98–1.02)	0.81	0.50 (0.41–0.59)	Retinal microcirculation

D-Dimer	1.00 (1.00–1.00)	0.26	0.49 (0.40–0.59)	Coagulation
INR	0.78 (0.01–85.07)	0.92	0.49 (0.41–0.57)	Coagulation
CXCL-10	1.00 (1.00–1.00)	0.95	0.49 (0.40–0.58)	Inflammation
Monocytes	0.91 (0.79–1.03)	0.17	0.45 (0.36–0.53)	Inflammation

Supplementary Table 11 Univariable logistic regression and receiver operating characteristic (ROC) analyses for discrimination of ME/CFS among previously infected individuals. Odds ratios (ORs) with 95% confidence intervals (CI) describe the association between each variable and ME/CFS status. Discriminatory performance is reported as area under the ROC curve (AUC) and the CI calculated using DeLongs´method. For each variable the biological domain is shown. Abbriviations: IL-6, interleukin-6; CRP, C-reactive protein; ICAM-1, intercellular adhesion molecule-1; VCAM-1, vascular cell adhesion molecule-1; LDL, low-density lipoprotein cholesterol; IgG, Immunoglobulin; TAG, triglycerides; aPTT, activated partial thromboplastin time; INR, international normalized ratio; MCP-1,Monocyte chemoattractant protein-1, CCL-5, C-C motif chemokine ligand 5; CXCL-10, C-X-C motif chemokine ligand 10; IL6, ICAM-1,VCAM-1, MCP-1,CCL-5, CXCL-10 all n=190, Statistical significance is indicated as *p < 0.05, **p < 0.01, and *** p < 0.001.

	Predictor	**Estimate**	**95% CI**	**p-value**
VCAM-1 (pg/mL)	Recovered	−2319.6	−3265.5 to −1373.7	**<0.001*** **
ICAM-1 (pg/mL)	Recovered	−358.9	−529.2 to −188.6	**<0.001*** **
IL-6 (pg/mL)	Recovered	−0.24	−0.56 to 0.08	0.14
MCP-1 (pg/mL)	Recovered	−3.52	−7.87 to 0.84	0.11

Supplementary Table 12 Values are regression coefficients with 95% confidence intervals derived from robust linear regression models (M-estimation). Models were adjusted for age. The renference cohort is the “recovered corhort”. Significance levels: ***p < 0.001



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Supplemental Figure 1 Spearman correlation heatmap between selected laboratory parameters and RVA metrics in PCS patients. Significant correlations ($p < 0.05$) after Benjamini–Hochberg FDR correction are shown. Spearman's ρ ranges from +1 (yellow) to −1 (blue).