Supplement: Plasma sCD14-ST Levels are Associated with COVID-19-Related Respiratory Failure

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Figure S1: Dot plot describing the relationship between sCD14-ST (x-axis) and sCD14 (y-axis) in COVID-19. Both biomarkers are log10 transformed and in pg/ml. Unadjusted linear regression was used to fit a line with 95% confidence intervals, and the p-values and r^2 values are reported.

Figure S2: In patients with COVID-19, dot plots describing the colinear relationship observed between sCD14 and other inflammatory biomarkers of interest in COVID-19. The x-axis denotes log10 transformed sCD14 levels in pg/ml. Y-axes display log10 transformed biomarkers (IL-6 pg/ml, sTREM pg/ml, sTNFR1 pg/ml, CRP mg/ml). Unadjusted linear regression was used to fit a line with 95% confidence intervals, and the p-values and r^2 values are reported.

Figure S3: In patients with COVID-19, dot plots describing the colinear relationship observed between sCD14 and admission WBC subpopulation counts. The x-axis denotes log10 transformed sCD14-ST or sCD14 levels both in pg/ml. Y-axes display log10 transformed neutrophil count (top), lymphocyte count (middle) and monocyte count (lower) all in k/µl. Unadjusted linear regression was used to fit a line with 95% confidence intervals, and the p-values and r^2 values are reported.

Supplemental Tables:

Table S1: Immunoassay quality control data.

Biomarker	Below LLOD n (%)	Above standard range n (%)	Interplate CV	Intraplate CV
sCD14	2 (0.01%)	1 (<0.01%)	10.5%	4.0%
sCD14-ST	4 (2%)	24 (12%)	10.1%	4.1%

Abbreviations: LLOD, lower limit of detection

Table S2: Sensitivity analysis describing the fold difference of sCD14-ST and sCD14 levels between COVID-19 negative and COVID-19 positive patients with PNA and/or respiratory failure

Plasma biomarkers	COVID-19 Negative (n=80) Median (IQR)	COVID-19 Positive (n=78) Median (IQR)	Unadjusted		Adjusted	
			Fold Difference (95% CI)	*p*	Fold Difference (95% CI)	*p*
sCD14-ST	12.5 (ng/ml) (3.5, 34.0)	4.9 (ng/ml) (1.4, 13.7)	0.40 (0.23-0.69)	*0.001*	0.49 (0.27-0.86)	*0.014*
sCD14	3.11 (mcg/ml) (2.04, 5.83)	3.18 (mcg/ml) (2.18, 4.28)	0.97 (0.79-1.19)	*0.80*	1.02 (0.72-1.72)	*0.91*

Adjusted model: age, gender, race/ethnicity, steroids, Charlson Comorbidity Index w/o age and SOFA
Abbreviations: 95% CI, 95% confidence interval.
The non-COVID-19 group is the reference for the fold difference calculation

Table S3: In COVID-19 patients only, association of sCD14 and sCD14-ST with clinical outcomes with additional model adjusting for culture verified bacterial infection.

Outcome	Plasma Biomarker	Unadjusted	*p*	*Adjusted Model*	*p*
Hospital Mortality (RR, 95% CI)	sCD14-ST	1.18 (1.06-1.32)	*0.003*	1.19 (1.04-1.38)	*0.013*
	sCD14	0.91 (0.72-1.16)	*0.46*	0.99 (0.77-1.30)	*0.97*
VFDs (Beta, 95% CI)	sCD14-ST	-0.11 (-0.17- -0.063)	*<0.0001*	-0.082 (-0.14- -0.026)	*0.005*
	sCD14	0.037 (-0.13- 0.20)	*0.65*	0.014 (-0.13- 0.16)	*0.85*
Shock (RR, 95% CI)	sCD14-ST	1.14 (1.07-1.22)	*<0.0001*	1.14 (1.06-1.23)	*<0.001*
	sCD14	0.92 (0.82-1.04)	*0.18*	0.92 (0.82-1.02)	*0.12*
Severe AKI* (RR, 95% CI)	sCD14-ST	1.20 (1.05-1.36)	*0.006*	1.21 (1.02-1.43)	*0.022*
	sCD14	0.83 (0.68-1.01)	*0.066*	0.83 (0.66-1.05)	*0.11*

Relative risk estimates are for a doubling of biomarker concentrations
Beta estimates are for change between VFD tertile per doubling of biomarker concentration
Adjusted model: age, gender, race/ ethnicity, steroids, Charlson Comorbidity, and culture verified bacterial infection
Abbreviations: 95% CI, 95% confidence interval; RR, relative risk; VFDs, ventilator free days; AKI, acute kidney injury
*Patients on HD prior to admission were excluded from severe AKI analysis

Table S4: Prevalence of culture verified bacterial or fungal infections in COVID-19 positive and COVID-19 negative patients by site and organism class.

	COVID-19 positive with culture verified infection (n=23)			COVID-19 negative with culture verified infection (n=35)		
	Total by site	Gram positive	Gram negative	Total by site	Gram positive	Gram negative
Bacteremia	3	3	0	11	4	7
Fungemia	0	0	0	2	NA	NA
Pulmonary infection	13	12	3	15	10	15
Urinary tract infection	5	1	5	9	3	7
Skin and soft tissue infection	3	1	3	2	2	0
Pharyngitis	1	1	0	0	0	0
Ascitic fluid infection	0	0	0	1	1	0

Some infections were polymicrobial and some patients had more than one infection

Abbreviations: SSTI, skin and soft tissue infection

Infections represented here were present upon enrollment or detected on day 0 or 1

Table S5: In COVID-19, association of sCD14 and sCD14-ST with VFDs with additional models adjusting for IL-6 and CRP.

Plasma Biomarker	Unadjusted Beta (95% CI)	p	Adjusted Model #1 Beta (95% CI)	p	Adjusted Model #2 Beta (95% CI)	p
sCD14-ST	-0.11 (-0.17- -0.063)	*<0.0001*	-0.075 (-0.13- -0.015)	*0.015*	*-0.10 (-0.16- -0.042)*	*0.001*
sCD14	0.037 (-0.13- 0.20)	*0.65*	-0.050 (-0.25- 0.15)	*0.97*	*-0.0021 (-0.22- 0.22)*	*0.98*

Beta estimates are for change between VFD tertile per doubling of biomarker concentration
Adjusted model #1: age, gender, race/ ethnicity, steroids, Charlson Comorbidity, and IL-6
Adjusted model #2: age, gender, race/ ethnicity, steroids, Charlson Comorbidity, and CRP
Abbreviations: 95% CI, 95% confidence interval; RR, relative risk; VFDs, ventilator free days

r^2=7.1e-4
p=0.79