

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Comparison of COVID-CS and COVID-CS Neg cohorts.

Characteristic	COVID-CS, N = 337	COVID-CS Neg, N = 8,695	p-value ¹
Ferritin			<0.001
Median (IQR)	3,490 (1,886, 5,927)	601 (246, 1,221)	
Unknown	1 (0.3%)	7,601 (87%)	
IL_6			<0.001
Median (IQR)	39 (16, 116)	20 (10, 48)	
Unknown	23 (6.8%)	8,325 (96%)	
CRP			<0.001
Median (IQR)	146 (95, 225)	62 (14, 135)	
Unknown	1 (0.3%)	7,494 (86%)	
ALT			<0.001
Median (IQR)	45 (27, 85)	24 (16, 40)	
Unknown	1 (0.3%)	5,626 (65%)	
Alk_Phos			<0.001
Median (IQR)	114 (86, 184)	93 (73, 125)	
Unknown	1 (0.3%)	5,671 (65%)	
Bili_Direct			<0.001
Median (IQR)	0.30 (0.20, 0.60)	0.20 (0.20, 0.30)	
Unknown	68 (20%)	7,528 (87%)	
Bili_Indirect			<0.001
Median (IQR)	0.60 (0.40, 0.90)	0.50 (0.40, 0.70)	
Unknown	68 (20%)	7,529 (87%)	
Bili_Total			<0.001
Median (IQR)	0.70 (0.50, 1.23)	0.50 (0.40, 0.70)	
Unknown	9 (2.7%)	6,016 (69%)	
Creatinine			<0.001
Median (IQR)	1.13 (0.85, 1.65)	0.93 (0.75, 1.17)	
Unknown	0 (0%)	5,463 (63%)	
D.Dimer			<0.001
Median (IQR)	2.8 (1.5, 7.3)	1.4 (0.7, 3.1)	
Unknown	22 (6.5%)	7,625 (88%)	
Fibrinogen			<0.001
Median (IQR)	335 (232, 450)	401 (316, 499)	
Unknown	20 (5.9%)	7,688 (88%)	
IL_2_Recp			0.9
Median (IQR)	2,609 (1,465, 7,628)	4,206 (1,028, 10,673)	
Unknown	319 (95%)	8,689 (100%)	
LDH			<0.001

Characteristic	COVID-CS, N = 337	COVID-CS Neg, N = 8,695	p-value ¹
Median (IQR)	429 (292, 656)	247 (197, 340)	
Unknown	3 (0.9%)	6,700 (77%)	
Lymphocyte_Abs			<0.001
Median (IQR)	1.02 (0.58, 1.69)	1.29 (0.85, 1.85)	
Unknown	3 (0.9%)	5,426 (62%)	
Monocyte_Abs			<0.001
Median (IQR)	0.74 (0.45, 1.28)	0.60 (0.45, 0.84)	
Unknown	3 (0.9%)	5,433 (62%)	
Neutrophil_Abs			<0.001
Median (IQR)	6.7 (4.1, 12.8)	4.2 (2.8, 6.6)	
Unknown	3 (0.9%)	5,426 (62%)	
Platelet_count			<0.001
Median (IQR)	65 (20, 128)	186 (125, 245)	
Unknown	1 (0.3%)	5,377 (62%)	
TNF_alpha			<0.001
Median (IQR)	25 (17, 44)	17 (11, 25)	
Unknown	121 (36%)	8,367 (96%)	
Troponin_T			<0.001
Median (IQR)	30 (16, 61)	18 (11, 32)	
Unknown	50 (15%)	7,800 (90%)	
V_Lactate			<0.001
Median (IQR)	1.60 (1.10, 2.50)	1.30 (0.90, 1.70)	
Unknown	151 (45%)	8,192 (94%)	
WBC			<0.001
Median (IQR)	2.30 (1.00, 4.00)	4.90 (3.30, 6.70)	
Unknown	0 (0%)	5,392 (62%)	
¹ Wilcoxon rank sum test; Wilcoxon rank sum exact test			

eTable 2: Summary of missingness

Characteristic	N = 671¹
WBC	0 (0%)
Neutrophil_Abs	29 (4.3%)
Lymphocyte_Abs	31 (4.6%)
Monocyte_Abs	33 (4.9%)
Hgb	0 (0%)
Platelet_count	0 (0%)
Fibrinogen	47 (7.0%)
D.Dimer	109 (16%)
CRP	74 (11%)
ESR	404 (60%)
Ferritin	7 (1.0%)
LDH	1 (0.1%)
IL_6	342 (51%)
IL_2_Recp	442 (66%)
TNF_alpha	458 (68%)
ALT	1 (0.1%)
Alk_Phos	1 (0.1%)
Bili_Total	3 (0.4%)
Bili_Direct	76 (11%)
Bili_Indirect	76 (11%)
Albumin_Lvl	1 (0.1%)
Creatinine	1 (0.1%)
Troponin_T	330 (49%)
Sodium_Lvl	0 (0%)
V_Lactate	357 (53%)

¹n (%)

eTable 3. Regression model (controlled for the effect of race, gender, and age) of laboratory values compared by cause of CS (COVID-CS, CAR-T CRS, and MA-HLH).

Lab	Covid-CS vs. CAR-T CRS	MA-HLH vs. CAR-T CRS	MA-HLH vs. Covid-CS
D.Dimer	<0.001	<0.001	<0.001
Albumin_Lvl	0.004	<0.001	<0.001
Ferritin	<0.001	<0.001	<0.001
Hgb	0.312	<0.001	<0.001
CRP	0.091	0.682	0.274
IL_6	0.092	0.086	<0.001
WBC	<0.001	0.001	<0.001
Fibrinogen	<0.001	<0.001	<0.001
TNF_alpha	0.017	<0.001	<0.001

eTable 4. Cox proportional hazards model regressing survival on demographic variables, and cohort.

Characteristic	HR ¹	95% CI ¹	p-value
Cohort			
CAR-T CRS	—	—	
COVID-CS	2.93	1.95, 4.41	<0.001
MA-HLH	8.12	5.51, 12.0	<0.001
Race			
Caucasian	—	—	
Other	1.12	0.80, 1.56	0.5
Black or AA	0.84	0.59, 1.21	0.4
Asian	1.13	0.67, 1.89	0.6
Gender			
F	—	—	
M	0.93	0.73, 1.18	0.5
Age	1.01	1.01, 1.02	<0.001
¹ HR = Hazard Ratio, CI = Confidence Interval			

eTable 5. Univariate Cox PH of laboratory values comparing CAR-T CRS, COVID-CS, and MA-HLH cohorts.

Characteristic	N	HR ¹	95% CI ¹	p-value
Gender	671			
F		—	—	
M		0.79	0.63, 1.00	0.054
Race	667			
Caucasian		—	—	
Other		1.14	0.82, 1.59	0.435
Black or AA		0.94	0.66, 1.36	0.758
Asian		1.31	0.79, 2.18	0.302
Age	671			
(0,50]		—	—	
(50,60]		0.97	0.70, 1.34	0.852
(60,70]		0.79	0.58, 1.07	0.128
(70,120]		0.95	0.69, 1.32	0.764
WBC	671	0.73	0.64, 0.83	<0.001
Neutrophil_Abs	642	0.78	0.69, 0.89	<0.001
Lymphocyte_Abs	640	0.87	0.76, 0.99	0.032
Monocyte_Abs	638	0.77	0.68, 0.88	<0.001
Hgb	671	0.57	0.51, 0.64	<0.001
Platelet_count	671	0.48	0.42, 0.54	<0.001
Fibrinogen	624	0.67	0.60, 0.76	<0.001
D.Dimer	562	1.92	1.69, 2.19	<0.001
CRP	597	1.30	1.14, 1.48	<0.001
ESR	267	1.02	0.86, 1.21	0.838
Ferritin	664	2.45	2.16, 2.79	<0.001
LDH	670	2.24	1.97, 2.55	<0.001
IL_6	329	1.69	1.42, 2.00	<0.001
IL_2_Recp	229	1.24	1.06, 1.44	0.006
TNF_alpha	213	1.46	1.19, 1.80	<0.001
ALT	670	1.44	1.27, 1.62	<0.001
Alk_Phos	670	1.85	1.64, 2.08	<0.001
Bili_Total	668	1.96	1.72, 2.22	<0.001
Bili_Direct	595	2.12	1.86, 2.40	<0.001
Bili_Indirect	595	1.49	1.31, 1.69	<0.001
Albumin_Lvl	670	0.58	0.52, 0.65	<0.001
Creatinine	670	1.34	1.20, 1.51	<0.001
Troponin_T	341	1.51	1.30, 1.75	<0.001

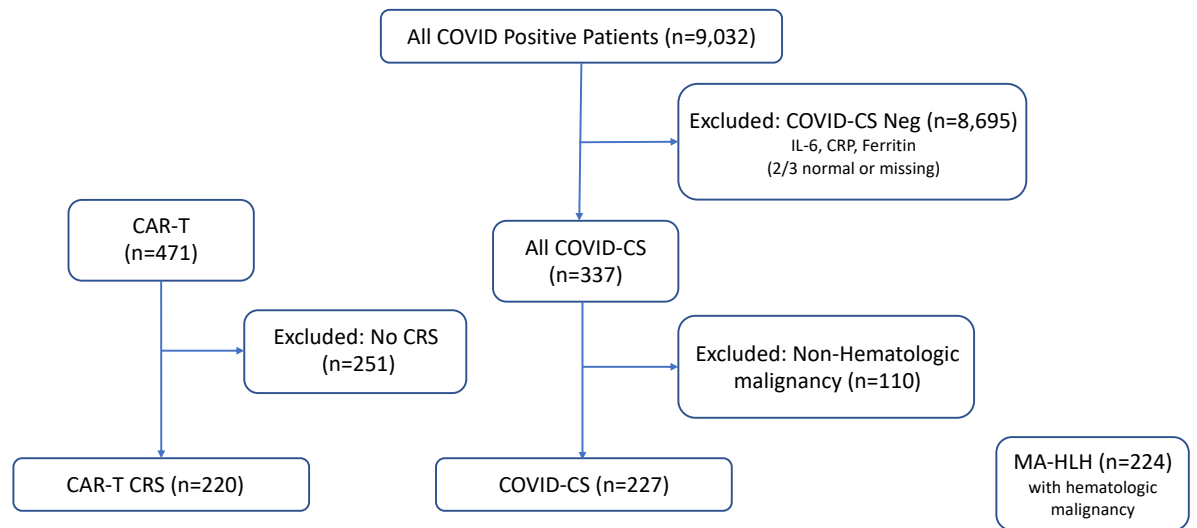
Characteristic	N	HR ¹	95% CI ¹	p-value
Sodium_Lvl	671	0.87	0.77, 0.98	0.018
V_Lactate	314	1.71	1.43, 2.04	<0.001
Cohort	671			
CAR-T CRS		—	—	
COVID-CS		2.92	1.94, 4.37	<0.001
MA-HLH		7.20	4.93, 10.5	<0.001
¹ HR = Hazard Ratio, CI = Confidence Interval. Abbreviations: Hazard ratios (HR), 95% confidence intervals (CI), and p-values.				

eTable 6. Multivariate Cox PH of laboratory values comparing CAR-T CRS, COVID-CS, and MA-HLH cohorts.

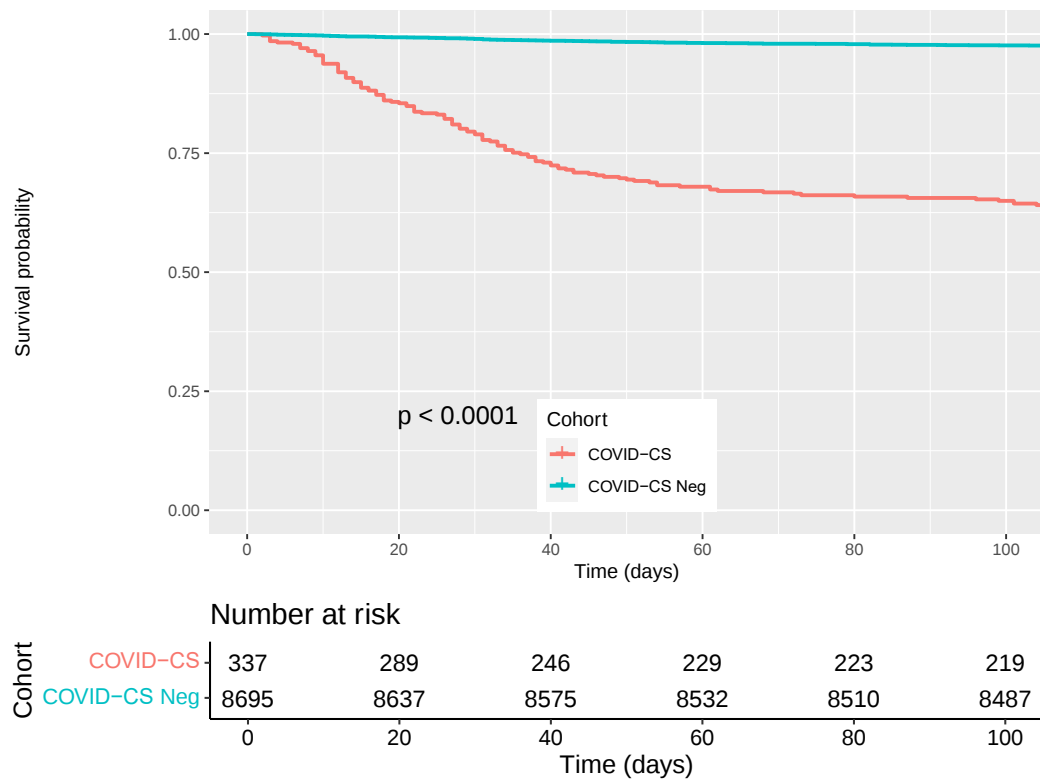
Characteristic	HR ¹	95% CI ¹	p-value
Gender			
F	—	—	
M	0.82	0.63, 1.06	0.13
Race			
Caucasian	—	—	
Other	1.12	0.79, 1.60	0.5
Black or AA	0.82	0.56, 1.20	0.3
Asian	1.48	0.86, 2.55	0.2
Age			
(0,50]	—	—	
(50,60]	1.35	0.96, 1.90	0.088
(60,70]	1.14	0.82, 1.60	0.4
(70,120]	1.75	1.21, 2.54	0.003
WBC	1.24	1.04, 1.48	0.016
Neutrophil_Abs	0.86	0.72, 1.02	0.088
Lymphocyte_Abs	0.99	0.84, 1.17	>0.9
Monocyte_Abs	0.98	0.81, 1.19	0.8
Hgb	1.13	0.94, 1.37	0.2
Platelet_count	0.57	0.47, 0.70	<0.001
Fibrinogen	0.95	0.82, 1.10	0.5
D.Dimer	1.04	0.88, 1.24	0.6
CRP	1.16	1.01, 1.35	0.038
ESR	0.91	0.73, 1.13	0.4
Ferritin	1.30	1.03, 1.63	0.025
LDH	1.36	1.13, 1.63	0.001
IL_6	1.38	1.13, 1.67	0.002
IL_2_Recp	1.09	0.90, 1.31	0.4
TNF_alpha	0.83	0.66, 1.06	0.13
ALT	0.85	0.72, 1.00	0.052
Alk_Phos	1.15	0.97, 1.36	0.11
Bili_Total	0.95	0.71, 1.26	0.7
Bili_Direct	1.38	1.02, 1.87	0.037
Bili_Indirect	0.98	0.79, 1.22	0.9
Albumin_Lvl	0.92	0.77, 1.09	0.3
Creatinine	1.06	0.93, 1.21	0.4
Troponin_T	1.16	0.96, 1.41	0.13

Characteristic	HR ¹	95% CI ¹	p-value
Sodium_Lvl	1.20	1.06, 1.35	0.003
V_Lactate	1.08	0.88, 1.32	0.5
Cohort			
CAR-T CRS	—	—	
COVID-CS	2.61	1.65, 4.12	<0.001
MA-HLH	2.55	1.57, 4.13	<0.001
¹ HR = Hazard Ratio, CI = Confidence Interval. Abbreviations: Hazard ratios (HR), 95% confidence intervals (CI), and p-values.			

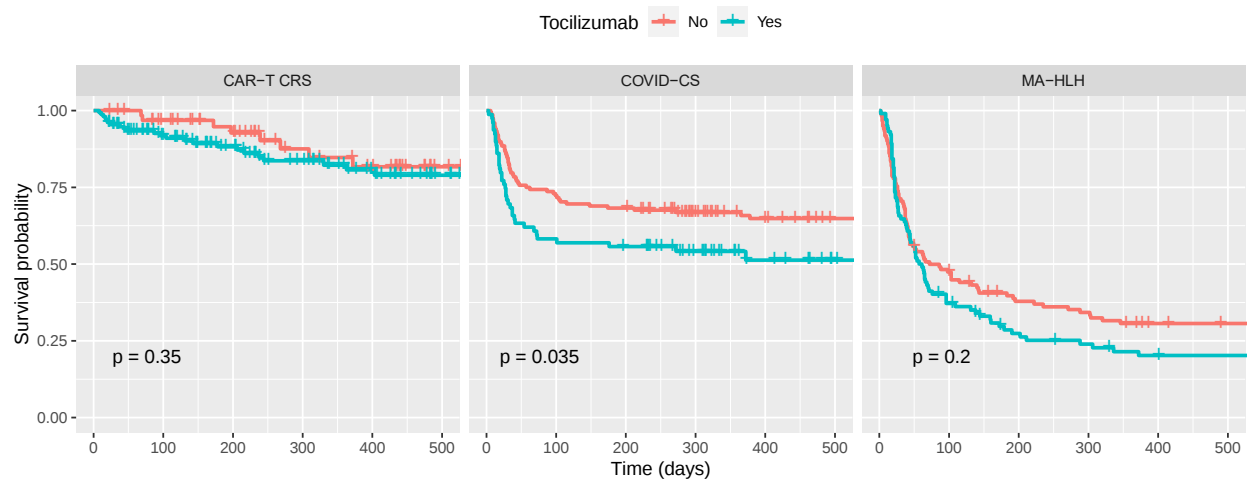
eFigure 1: Flow Diagram



eFigure 2: Comparison of survival between COVID-19 patients diagnosed with Cytokine Storm (COVID-CS) and COVID-19 patients not diagnosed with cytokine storm (COVID-CS Neg).



eFigure 3: Association of tocilizumab with overall survival by cohort.



eFigure 4: Variable importance in the Random Survival Forest (RSF) model. Higher variable importance implies the variable has a larger impact on prediction performance.

