

SUPPLEMENTAL MATERIAL FOR: Autopsy Findings from Patients Diagnosed with COVID-19 Demonstrate Unique Morphologic Patterns in Bone

Marrow and Lymph Node

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Supplemental Figure 1.

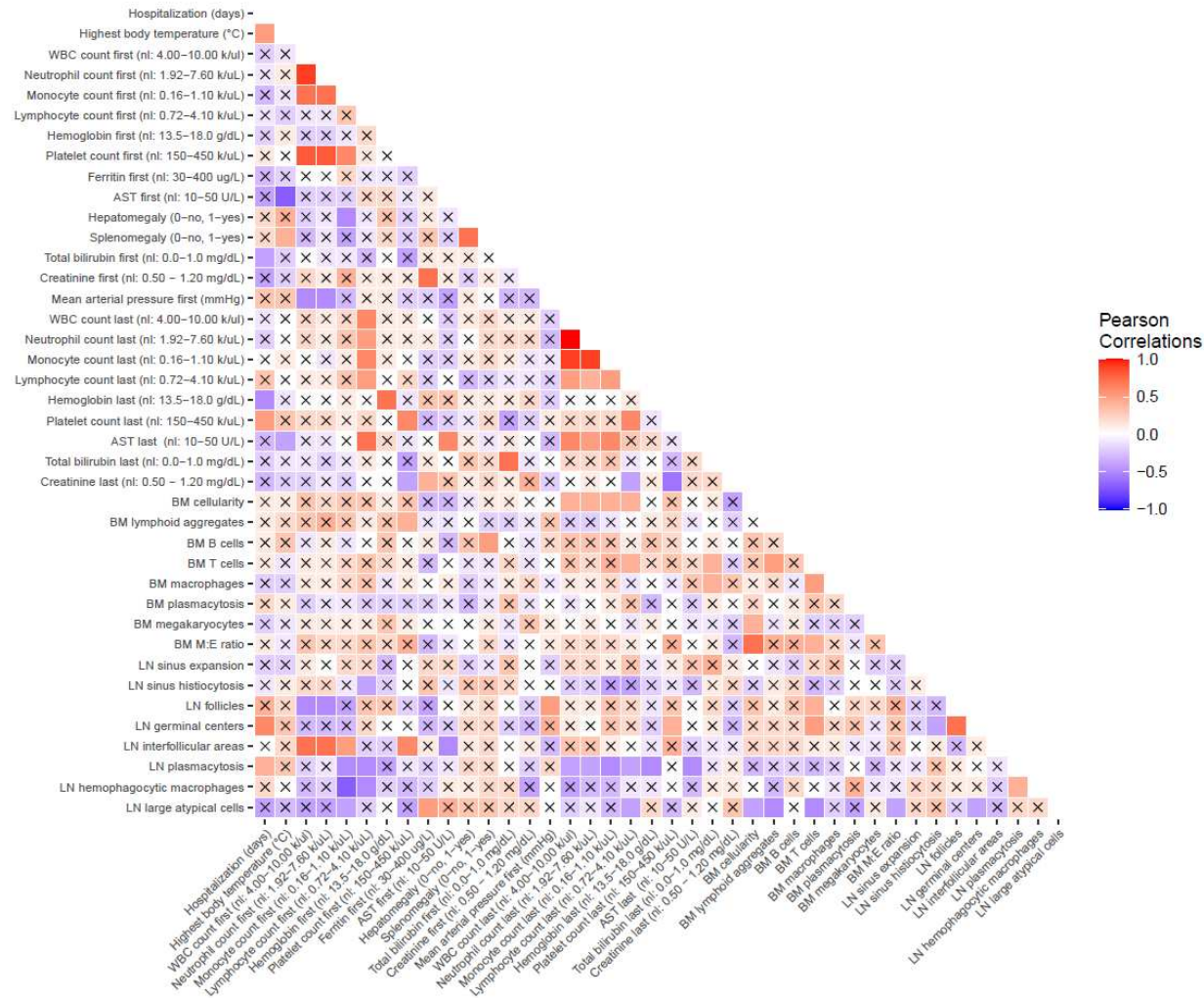


Figure Legend: The heatmap represents all pairwise comparisons, excluding the diagonal, between the scaled and centered clinical, morphological, and hematological parameters measured in our sample of the patients with severe COVID. All pairwise comparisons were estimated as Pearson correlation coefficients. The range of these coefficients spans from -1 in blue, representing a negative correlation, to +1 in red, representing a positive correlation. No correlation, a coefficient of 0, is represented by white. The significance of these pairwise comparison is indicated by their obfuscation - that is all non-significant comparisons are labeled with an "X". Significance was declared at the 5% type I error using a t-test.

Supplementary Table 1: Factors associated with BM hemophagocytic macrophages

		Median*		Wilcoxon Rank-Sum Test				
		BM Hemophagocytic macrophages		Difference	95% CI Lower Bound	95% CI Upper Bound	p-value	FDR
		Yes (N=9)	No (N=16)					
Overall Hospitalization parameters	Hospitalization (days)	20.00	9.50	-8.34	-16.00	0.00	0.050	0.570
	Highest body temperature (°C)	39.60	38.90	-0.70	-1.30	0.30	0.125	0.752
Laboratory Parameters at initial hospitalization	WBC count first (nl: 4.00-10.00 k/uL)	4.83	8.05	2.07	-1.96	5.32	0.419	0.752
	Neutrophil count first (nl: 1.92-7.60 k/uL)	3.30	6.12	2.30	-1.04	4.48	0.388	0.752
	Monocyte count first (nl: 0.16-1.10 k/uL)	0.25	0.49	0.17	-0.11	0.57	0.350	0.752
	Lymphocyte count first (nl: 0.72-4.10 k/uL)	0.60	0.82	0.21	-0.23	0.80	0.350	0.752
	Hemoglobin first (nl: 13.5-18.0 g/dL)	12.40	13.35	1.00	-3.50	3.50	0.552	0.807
	Platelet count first (nl: 150-450 k/uL)	128.00	164.50	17.50	-39.00	73.00	0.637	0.807
	Ferritin first (nl: 30-400 ug/L)	266.00	687.00	324.50	-92.00	1149.00	0.179	0.752
	AST first (nl: 1+BS:1480-50 U/L)	35.00	44.00	10.00	-13.00	59.00	0.428	0.752
	Total bilirubin first (nl: 0.0-1.0 mg/dL)	0.50	0.40	-0.20	-1.40	0.10	0.391	0.752
	Triglyceride first (nl: 35-150 mg/dL)	258.50	235.00	1.41	-249.00	205.00	1.000	1.000
	Creatinine first (nl: 0.50 - 1.20 mg/dL)	1.01	1.36	0.24	-0.36	1.42	0.411	0.752
	C-reactive protein first (nl: 0-10 mg/L)	107.10	72.45	7.40	-97.90	132.50	0.904	0.996
	INR first (nl: 0.9-1.1)	1.10	1.20	0.05	-0.40	0.20	0.636	0.807
	Fibrinogen first (nl: 200-450 mg/dL)	544.50	561.50	-117.50	-280.00	122.00	0.624	0.807
Clinical Parameters at initial hospitalization	FiO2 first (%)	60.00	60.00	0.00	-30.00	50.00	1.000	1.000
	Mean arterial pressure first (mmHg)	91.00	93.00	1.00	-15.00	15.00	1.000	1.000
	PaO2 first (nl: 65-95 mmHg)	99.00	88.00	-26.00	-72.00	9.00	0.174	0.752
	SOFA first	6.50	10.00	3.00	-3.00	9.00	0.343	0.752
Laboratory Parameters at Demise	WBC count last (nl: 4.00-10.00 k/uL)	11.65	11.92	0.20	-5.98	6.84	1.000	1.000
	Neutrophil count last (nl: 1.92-7.60 k/uL)	8.36	8.92	0.51	-4.93	6.25	1.000	1.000
	Hepatomegaly (0-no, 1=yes)	1.00	0.00	-1.00	-1.00	0.00	0.601	0.807
	Splenomegaly (0-no, 1=yes)	1.00	1.00	0.00	-1.00	0.00	0.307	0.752
	Monocyte count last (nl: 0.16-1.10 k/uL)	0.81	0.41	-0.29	-0.68	0.23	0.371	0.752
	Lymphocyte count last (nl: 0.72-4.10 k/uL)	1.18	0.79	-0.18	-1.01	0.59	0.571	0.807
	Hemoglobin last (nl: 13.5-18.0 g/dL)	8.50	9.60	1.00	-0.60	3.80	0.325	0.752
	Platelet count last (nl: 150-450 k/uL)	259.00	160.00	-73.00	-206.00	90.00	0.446	0.752
	Ferritin last (nl: 30-400 ug/L)	612.00	1669.00	1010.50	86.00	7296.00	0.028	0.424
	AST last (nl: 10-50 U/L)	34.00	74.50	39.89	2.00	96.00	0.023	0.424
	Total bilirubin last (nl: 0.0-1.0 mg/dL)	0.50	0.60	-0.10	-3.40	0.60	0.568	0.807
	Triglyceride last (nl: 35-150 mg/dL)	212.00	252.00	73.50	-98.00	301.00	0.456	0.752
	Creatinine last (nl: 0.50 - 1.20 mg/dL)	1.49	2.75	0.75	-0.64	2.08	0.245	0.752
	C-reactive protein last (nl: 0-10 mg/L)	44.40	124.30	73.80	-61.70	255.60	0.124	0.752
INR last (nl: 0.9-1.1)	1.20	1.45	0.20	-0.22	0.50	0.259	0.752	
Fibrinogen last (nl: 200-450 mg/dL)	664.00	483.00	-169.50	-358.00	30.00	0.152	0.752	
Clinical Parameters at Demise	FiO2 last (%)	55.25	60.00	0.01	-30.00	40.00	0.765	0.909
	Mean arterial pressure last (mmHg)	59.50	78.00	7.00	-15.00	46.00	0.491	0.778
	PaO2 last (nl: 65-95 mmHg)	80.00	87.00	-3.85	-50.00	31.00	0.814	0.947
	SOFA last	9.50	13.00	2.00	-5.00	7.00	0.237	0.752
Autopsy BM findings	BM cellularity	80.00	72.50	-5.00	-25.00	5.00	0.196	0.752
	BM B cells	2.93	3.04	0.07	-0.30	0.58	0.571	0.807
	BM T cells	5.00	4.25	-0.50	-1.50	0.50	0.345	0.752
	BM macrophages	5.50	5.25	0.00	-1.00	0.50	0.462	0.752
	BM plasmacytosis	6.50	5.50	-0.50	-2.50	0.50	0.312	0.752
	BM M:E ratio	5.50	5.50	0.00	-1.50	0.00	0.334	0.752
Autopsy LN findings	LN sinus expansion	6.00	6.00	0.00	-0.50	0.50	0.838	0.956
	LN sinus histiocytosis	6.00	6.00	0.00	-0.50	1.00	0.622	0.807
	LN follicles	6.50	5.00	-1.00	-2.00	0.00	0.167	0.752
	LN germinal centers	5.00	0.00	-1.50	-5.50	0.00	0.030	0.424
	LN interfollicular expansion	3.50	3.50	0.00	-0.50	0.50	0.677	0.835
	LN plasmacytosis	4.00	2.00	-1.50	-2.00	0.00	0.019	0.424
	LN large atypical cells	5.00	6.00	1.00	0.00	1.50	0.062	0.590

*Median value for this histologic category.

Abbreviations and definitions: AST – aspartate aminotransferase, BM - bone marrow, FiO₂ - fraction of inspired oxygen, first – the first available clinical data on the patient at the time of hospitalization, INR - international normalised ratio, last – the last available clinical data on the patient prior to demise, LN – lymph node, m-score - the morphology score on a 8-point scale, PaO₂ - Partial pressure of oxygen, SOFA - Sequential Organ Failure Assessment, WBC – white blood cell .

Supplementary Table 2: Factors associated with LN plasmacytosis

		Median*		Wilcoxon Rank-Sum Test				
		LN Plasmacytosis		Difference	95% CI Lower Bound	95% CI Upper Bound	p-value	FDR
		Yes (N=20)	No (N=5)					
Overall Hospitalization parameters	Hospitalization (days)	13.00	3.00	9.00	-1.00	17.00	0.082	0.315
	Highest body temperature (°C)	39.05	38.30	0.80	0.00	1.70	0.071	0.315
Laboratory Parameters at initial hospitalization	WBC count first (nl: 4.00-10.00 k/u/L)	6.02	10.08	-1.47	-6.68	4.27	0.488	0.719
	Neutrophil count first (nl: 1.92-7.60 k/u/L)	4.16	5.98	-0.19	-4.08	3.71	0.921	0.988
	Monocyte count first (nl: 0.16-1.10 k/u/L)	0.25	0.80	-0.47	-1.05	-0.17	0.016	0.209
	Lymphocyte count first (nl: 0.72-4.10 k/u/L)	0.59	1.25	-0.65	-1.39	0.13	0.096	0.315
	Hemoglobin first (nl: 13.5-18.0 g/dL)	12.10	13.80	-2.70	-7.00	0.70	0.110	0.343
	Platelet count first (nl: 150-450 k/u/L)	155.50	156.00	11.00	-59.00	57.00	0.717	0.909
	Ferritin first (nl: 30-400 ug/L)	456.50	724.00	-310.00	-6358.00	286.00	0.257	0.542
	AST first (nl: 10-50 U/L)	37.50	70.00	-32.90	-85.00	19.00	0.208	0.455
	Total bilirubin first (nl: 0.0-1.0 mg/dL)	0.40	0.70	-0.10	-1.20	0.30	0.430	0.705
	Triglyceride first (nl: 35-150 mg/dL)	255.00	208.00	0.49	-1579.00	245.00	1.000	1.000
	Creatinine first (nl: 0.50 - 1.20 mg/dL)	1.30	1.33	-0.08	-2.10	0.94	0.812	0.952
	C-reactive protein first (nl: 0-10 mg/L)	118.10	48.00	56.00	-47.80	181.80	0.306	0.583
	INR first (nl: 0.9-1.1)	1.15	1.25	0.00	-0.40	0.50	0.897	0.988
	Fibrinogen first (nl: 200-450 mg/dL)	572.00	309.00	192.00	-217.00	407.00	0.479	0.719
	Clinical Parameters at initial hospitalization	Splenomegaly (0-no, 1-yes)	1.00	1.00	0.00	0.00	1.00	0.870
FiO2 first (%)		50.00	100.00	-26.57	-60.00	10.00	0.160	0.394
Mean arterial pressure first (mmHg)		92.50	80.00	8.00	-28.00	23.00	0.614	0.861
PaO2 first (nl: 65-95 mmHg)		91.50	94.00	4.30	-17.00	68.00	0.958	0.989
SOFA first		6.50	12.00	-6.00	-12.00	1.00	0.081	0.315
Laboratory Parameters at Demise	WBC count last (nl: 4.00-10.00 k/u/L)	11.06	18.81	-9.56	-51.90	-1.45	0.018	0.209
	Neutrophil count last (nl: 1.92-7.60 k/u/L)	7.62	16.92	-8.81	-31.14	-1.37	0.023	0.224
	Monocyte count last (nl: 0.16-1.10 k/u/L)	0.74	1.14	-0.63	-4.32	0.10	0.096	0.315
	Lymphocyte count last (nl: 0.72-4.10 k/u/L)	0.70	1.69	-0.71	-1.95	0.46	0.175	0.397
	Hemoglobin last (nl: 13.5-18.0 g/dL)	8.65	13.40	-3.62	-8.40	0.20	0.075	0.315
	Platelet count last (nl: 150-450 k/u/L)	189.00	161.50	23.50	-105.00	234.00	0.627	0.861
	Ferritin last (nl: 30-400 ug/L)	662.00	7922.00	-6892.50	-9032.00	-343.00	0.033	0.278
	AST last (nl: 10-50 U/L)	44.50	389.00	-344.32	-1435.00	-51.00	0.018	0.209
	Total bilirubin last (nl: 0.0-1.0 mg/dL)	0.50	4.80	-3.70	-4.60	0.00	0.060	0.315
	Triglyceride last (nl: 35-150 mg/dL)	212.00	367.00	-155.00	-1198.00	135.00	0.295	0.583
	Creatinine last (nl: 0.50 - 1.20 mg/dL)	2.00	2.97	-0.84	-2.15	0.87	0.333	0.595
	C-reactive protein last (nl: 0-10 mg/L)	79.90	202.05	-63.84	-299.80	195.90	0.323	0.595
	INR last (nl: 0.9-1.1)	1.30	3.00	-1.00	-2.80	1.30	0.086	0.315
	Fibrinogen last (nl: 200-450 mg/dL)	496.00	412.00	145.50	-370.00	396.00	0.476	0.719
	Clinical Parameters at Demise	FiO2 last (%)	60.00	51.00	9.00	-49.50	49.00	0.770
Mean arterial pressure last (mmHg)		75.00	62.00	3.49	-43.00	52.00	0.823	0.952
PaO2 last (nl: 65-95 mmHg)		73.00	95.00	-31.00	-61.00	14.00	0.154	0.394
SOFA last		11.00	15.00	-4.00	-8.00	3.00	0.169	0.397
Autopsy BM findings	BM cellularity	77.50	80.00	-5.00	-20.00	10.00	0.535	0.770
	BM lymphoid aggregates	0.00	0.00	0.00	-1.00	0.00	0.383	0.646
	BM B cells	2.94	3.32	-0.39	-1.05	0.05	0.066	0.315
	BM T cells	4.50	5.50	-1.00	-2.00	0.50	0.122	0.361
	BM Macrophages	5.25	5.50	-0.50	-1.50	0.00	0.147	0.394
	BM plasmacytosis	2.00	2.00	0.00	-1.00	2.00	0.915	0.988
	BM M:E ratio	5.50	5.50	0.00	-0.50	0.00	0.362	0.629
	LN sinus expansion	6.00	6.00	0.00	-0.50	0.50	0.972	0.989
Autopsy LN findings	LN sinus histiocytosis	6.00	5.50	0.50	0.00	1.00	0.144	0.394
	LN follicles	5.50	5.00	0.00	-1.50	1.50	0.972	0.989
	LN germinal centers	0.50	0.00	0.00	-3.50	1.50	0.686	0.909
	LN interfollicular areas	3.50	3.50	0.00	-1.00	0.50	0.748	0.919
	LN plasmacytosis	6.50	3.00	3.00	2.00	4.00	0.001	0.035
	LN large atypical cells/multinucleated/hyperchromatic cells	5.50	5.00	0.00	-1.00	1.50	0.700	0.909

*Median value for this histologic category.

Abbreviations and definitions: AST – aspartate aminotransferase, BM - bone marrow, FiO₂ - fraction of inspired oxygen, first – the first available clinical data on the patient at the time of hospitalization, INR - international normalized ratio, last – the last available clinical data on the patient prior to demise, LN – lymph node, m-score - the morphology score on a 8-point scale, PaO₂ - Partial pressure of oxygen, SOFA - Sequential Organ Failure Assessment, WBC – white blood cell .

