

**Supplement to An ALLY in fighting COVID-19: Magnitude of Albumin Decline and Lymphopenia (ALLY)
Predict Progression to Critical Disease**

Supplemental Table 1: Additional Baseline Results

Variable	Disease Severity on Admission:			P-value
	Moderate (N=59)	Serious (N=34)	Critical (N=10)	
Clinical Presentation				
Clinical Score	3 [3, 5]	4 [3, 5]	3 [2, 4]	0.61
Anorexia	8 (13.6%)	10 (29.4%)	4 (40%)	0.05
Chest Pain	10 (17.0%)	3 (8.8%)	1 (10%)	0.63
Cough	44 (74.6%)	30 (88.2%)	7 (70%)	0.22
Diarrhea	14 (23.7%)	9 (26.5%)	3 (30%)	0.84
Fever	47 (79.7%)	28 (82.4%)	8 (80%)	1.00
Headache	11 (18.6%)	4 (11.8%)	0 (0%)	0.38
Myalgia	4 (6.8%)	9 (26.5%)	3 (30%)	0.78
Rash	0 (0%)	1 (2.9%)	0 (0%)	0.43
Shortness of Breath	40 (67.8%)	25 (73.5%)	5 (50%)	0.38
Nausea/Vomiting	15 (25.4%)	8 (23.5%)	2 (20%)	1.00
Laboratory Features				
BNP (pg/mL)	51 [18, 118]	48 [22, 124]	82 [48, 129]	0.61
Total Bilirubin (mg/dL)	0.5 [0.4, 0.7]	0.6 [0.4, 0.9]	0.6 [0.3, 0.8]	0.76
Troponin-I (ng/mL)	0.02 [0.01, 0.02]	0.02 [0.01, 0.05]	0.04 [0.02, 0.06]	0.24
Admission Details				
Covid-19 RT-PCR Specimen Source, Nasopharyngeal	55 (93.2%)	33 (97.1%)	10 (100%)	0.79
Readmission, 30-day	2 (3.4%)	5 (14.7%)	1 (10%)	0.11
IMV Duration (d)	8 [7, 25]	16 [9, 29]	14 [6, 18]	0.51

Supplemental Table 2: Comparison of demographic, clinical, and laboratory factors between training and validation cohorts

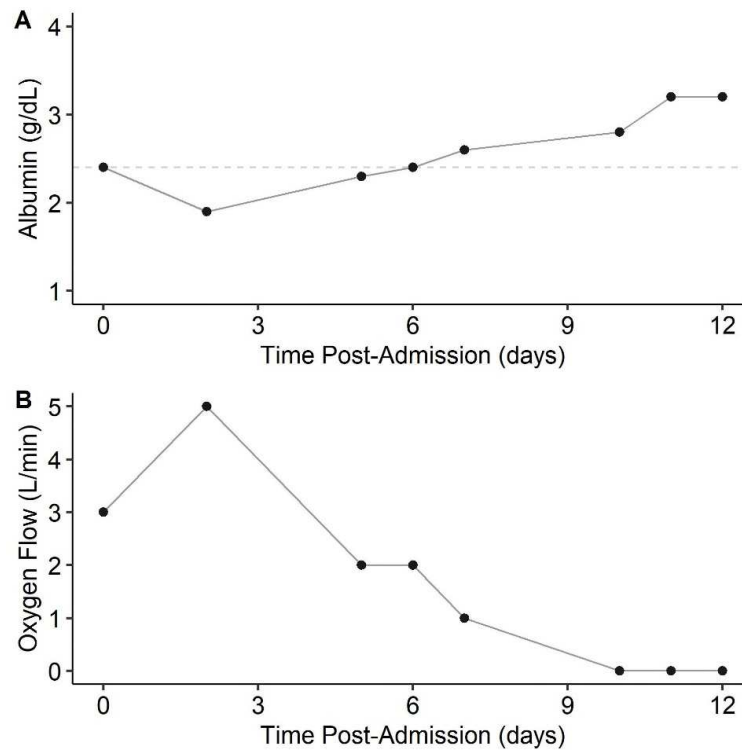
Variable	Cohort		P-value
	Derivation (N=93)	Validation (N=60)	
Demographics			
Age (y)	58 [49, 67]	71 [52, 86]	0.001
BMI (kg·m ⁻²)	30.9 [26.7, 36.0]	28.3 [24.3, 34.2]	0.16
Ethnicity, Hispanic or Latino	22 (23.7%)	15 (25.0%)	0.99
Male Gender	56 (60.2%)	30 (50%)	0.28
Race			0.52
Black or African American	32 (34.4%)	17 (28.3%)	
White or Caucasian	52 (55.9%)	39 (65%)	
Other	9 (9.7%)	4 (6.7%)	
Admission Clinical Presentation			
Blood Pressure, Systolic (mmHg)	130 [117, 147]	133 [121, 144]	0.69
Blood Pressure, Diastolic (mmHg)	77 [69, 86]	76 [66, 85]	0.31
Clinical Score	3 [3, 5]	3 [2, 4]	0.13
Anorexia	18 (19.4%)	10 (16.7%)	0.84
Chest Pain	13 (14.0%)	7 (11.7%)	0.87
Cough	74 (79.6%)	44 (73.3%)	0.48
Diarrhea	23 (24.7%)	10 (16.7%)	0.33
Fever	75 (80.7%)	46 (76.7%)	0.70
Headache	15 (16.1%)	9 (15.0%)	1.00
Myalgia	29 (68.8%)	17 (28.3%)	0.85
Rash	1 (1.1%)	0 (0%)	1.00
Shortness of Breath	56 (69.9%)	39 (65.0%)	0.65
Nausea/Vomiting	23 (24.7%)	13 (21.7%)	0.81
Respiratory Rate	20 [18, 22]	20 [18, 24]	0.46
SpO ₂ (%)	95 [94, 97]	96 [94, 98]	0.37
Comorbidities			
Comorbidity Score	1 [1, 3]	2 [1, 3]	0.05
Asthma	10 (10.8%)	7 (11.7%)	1.00
CAD	8 (8.6%)	10 (16.7%)	0.21

Cancer	10 (10.8%)	9 (15.0%)	0.60
COPD	7 (7.5%)	8 (13.3%)	0.37
Diabetes	31 (33.3%)	18 (30%)	0.80
Hypertension	53 (57.0%)	39 (65.0%)	0.41
Renal Disease	18 (19.4%)	17 (28.3%)	0.27
Smoker	28 (30.1%)	22 (36.7%)	0.50
Disease Severity on Admission			0.96
Moderate	59 (63.4%)	37 (61.7%)	
Serious	34 (36.6%)	23 (38.3%)	
Laboratory Results			
Albumin (on Admission) (g/dL)	3.5 [3.1, 3.9]	3.4 [3.1, 3.6]	0.19
Albumin Change (Baseline to Nadir) (g/dL)	-0.6 [-0.8, -0.4]	-0.4 [-0.7, -0.2]	0.04
Alkaline Phosphatase (U/L)	80 [59, 100]	85 [69, 105]	0.08
ALT (U/L)	32 [25, 54]	29 [18, 48]	0.05
AST (U/L)	39 [25, 58]	30 [24, 53]	0.13
BNP (pg/mL)	48 [21, 118]	49 [11, 148]	0.98
Creatinine (mg/dL)	1.0 [0.9, 1.4]	1.1 [0.9, 1.6]	0.29
C-reactive Protein (mg/dL)	6.0 [3.1, 12.7]	8.0 [1.6, 11.5]	0.34
Ferritin (ng/mL)	435 [240, 969]	406 [191, 563]	0.64
Lymphocytes (%)	18 [11, 24]	16 [10, 23]	0.25
Neutrophils (%)	72 [65, 82]	76 [67, 83]	0.29
Total Bilirubin (mg/dL)	0.5 [0.4, 0.7]	0.5 [0.4, 0.7]	0.17
Troponin-I (ng/mL)	0.02 [0.01, 0.03]	0.02 [0.02, 0.04]	0.50
Critical Outcomes			
Progression to critical disease	18 (19.4%)	10 (16.7%)	0.84
Invasive Mechanical ventilation	18 (19.4%)	9 (15.0%)	0.64
Multi-organ Failure	18 (19.4%)	7 (11.7%)	0.30
Shock	13 (14.0%)	11 (18.3%)	0.62
Mortality, inpatient	11 (11.8%)	12 (20.0%)	0.25

Abbreviations: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BNP, B-type Natriuretic Peptide; BMI, Body Mass Index; CAD, Coronary Artery Disease; COPD, Chronic Obstructive Pulmonary Disease; SpO₂, Pulse Oximeter Oxygen Saturation;

Figure Legends**Supplemental Figure S1: Illustration of Albumin Recovery.**

(A) Change of albumin over time from admission at day 0 to day 12 is presented as an illustrative case report for a patient admitted with serious COVID-19 disease. The largest delta albumin within 5 days is -0.5 at day 2. Albumin recovers above admission levels to 3.2g/dL at day 11. **(B)** Oxygen flow support by nasal cannula over time. Successful weaning to room air was achieved by day 11.

**Supplemental Figure S1**

Supplemental Table 3: Comparison of the largest delta albumin pre-critical disease status by progression of disease in derivation and validation groups

Variable	Disease Progression:		P-value
	Remained Non-Critical (N=125)	Progressed to Critical (N=28)	
Laboratory Results			
Albumin change within 5 days (Baseline to nadir) (g/dL)	-0.5 [-0.7, -0.3]	-0.7 [-0.9, -0.4]	0.007

Supplemental Table 4: Sensitivity analysis of ALLY model prediction in derivation and validation groups

Analysis	Sensitivity	Specificity	AUC (95% CI)
Main Analysis: Delta Albumin within 5 days and Baseline Lymphocyte			
Overall: Derivation and Validation	0.75	0.72	0.80 (0.70, 0.89)
Sensitivity Analysis: Pre-critical state Delta Albumin within 5 days and Baseline Lymphocyte			
Overall: Derivation and Validation	0.72	0.72	0.76 (0.66, 0.86)

Supplemental Table 5: Logistic regression models with total albumin change (baseline to nadir) adjusting for other potential predictors.

Variable	Estimate	SE	Odds Ratio (95% CI)	P-value
Model S1				
Anorexia	1.29	0.68	3.63 (0.95, 14.06)	0.057
Δ Albumin (g/dL)	-3.08	0.94	0.05 (0.01, 0.25)	0.001
Model S2				
Diabetes Mellitus	1.04	0.61	2.82 (0.87, 9.78)	0.09
Δ Albumin (g/dL)	-3.12	0.94	0.04 (0.01, 0.24)	<0.001
Model S3				
Serious vs. Moderate Disease on Admission	2.10	0.69	8.16 (2.29, 35.89)	0.002
Δ Albumin (g/dL)	-2.99	0.99	0.05 (0.01, 0.30)	0.003
Model S4				
SPO ₂ (%)	-0.21	0.09	0.81 (0.67, 0.95)	0.01
Δ Albumin (g/dL)	-3.17	1.00	0.04 (0, 0.25)	0.001
Model S5*				
CRP (mg/dL)	0.17	0.06	1.19 (1.06, 1.38)	0.008
Δ Albumin (g/dL)	-3.30	1.36	0.04 (0, 0.40)	0.02
Model S6**				
Ferritin (ng/mL)	0.00	0.00	1.00 (1.00, 1.00)	0.047

Δ Albumin (g/dL)	-3.98	1.34	0.02 (0, 0.18)	0.003
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Model S7

Neutrophil (%)	0.09	0.03	1.10 (1.03, 1.18)	0.008
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Δ Albumin (g/dL)	-3.05	0.99	0.05 (0.01, 0.27)	0.002
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Model S8

Total bilirubin (mg/dL)	1.91	0.98	6.75 (0.97, 49.0)	0.051
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Δ Albumin (g/dL)	-3.52	1.02	0.03 (0.00, 0.18)	<0.001
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* Baseline CRP was not performed in all patients (n = 52/93 in derivation set with CRP)

* Baseline Ferritin was not performed in all patients (n = 45/93 in derivation set with Ferritin)

Δ Albumin (g/dL) = Total Albumin Change (baseline to nadir); CRP= C-Reactive Protein; SE = Standard Error; SPO₂ = Pulse Oximeter Oxygen Saturation;