Assessing immune cell recovery and inflammatory markers as predictors for COVID outcomes

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Background

- COVID mortality has been associated with specific demographics (male, over 65 years old, African American), comorbidities (diabetes, congestive heart failure, pulmonary chronic conditions), and socioeconomic factors (low income, uninsured, and homelessness)
- However, easily attainable clinical correlates that can reliably predict disease outcome are lacking
- Fatal complications of COVID19, such as acute respiratory disease syndrome (ARDS) and sepsis, are often mediated by pathological inflammation in response to infection

Objectives:

- To identify and assess whether inflammatory biomarkers can predict clinical outcomes in COVID patients.
- To also track changes in immune cell composition that correlate with increased survival rates.

Methods

Study cohort

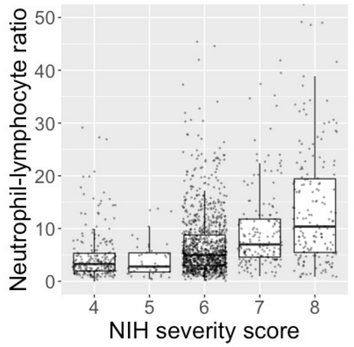
- Includes all patients admitted to UCLA Ronald Reagan Medical Center and Santa Monica Medical Center from Jan 2020 to Jan 2021.
- Patients tested positive for COVID onsite via PCR test
- Children (<18 y.o.) were excluded from the study cohort
- Final number of patients after exclusion: n=1832

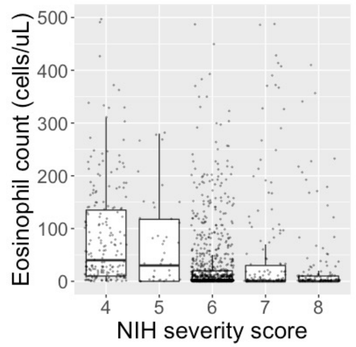
Analysis

- Lab values, patient demographics, comorbidities, treatments, and outcomes all imported from REDCap linked to UCLA electronic health records
- Survival analysis was performed using statistical packages 'ggplot2' and 'survminer' on R

Results/Analysis

Figure 1: Elevated neutrophil-lymphocyte ratio (NLR) and eosinopenia at admission are associated with poor clinical outcomes





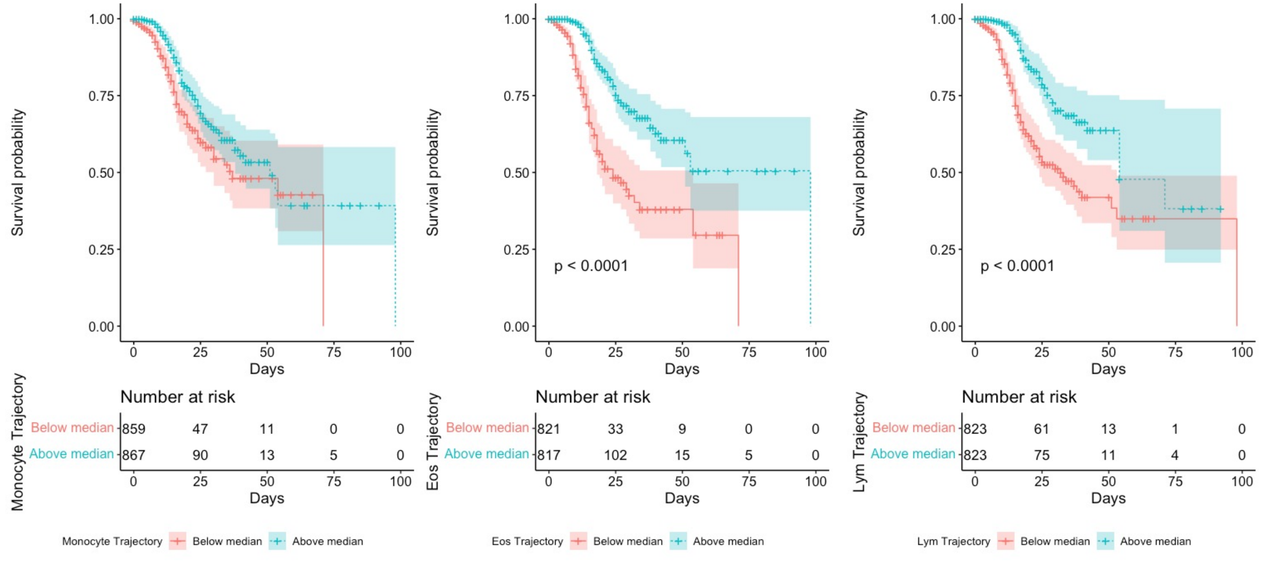
NIH severity scale	Requirements
4	Hospitalized; not requiring supplemental O2
5	Hospitalized; requiring any supplemental O2
6	Hospitalized; requring noninvasive ventilation or use of high-flow oxygen devices
7	Hosptialized; receiving invasive mech. Ventilation or ECMO
8	Death

Figure 2: Patients who succumb to COVID have increased inflammatory markers at admission and during hospitalization

Inflammatory markers (admission)	Live (n=1611)	Dead (n=201)	
	Median (IQR)	*Median (IQR)*	*p-value*
Ferritin (ng/mL)	552 (892)	973 (1385)	<0.001
D-dimer (ng/mL)	910 (1235)	2335 (4518)	<0.001
IL-6 (pg/mL)	5.35 (13.83)	22 (55)	<0.001
Procalcitonin (ng/mL)	0.13 (0.33)	0.50 (1.73)	<0.001
C-reactive protein (mg/L)	6.20 (9.10)	11.70 (10.25)	<0.001

Change in inflammatory markers during hospitalization	Live (n=1611)	Dead (n=201)	
	Mean (SD)	*Mean (SD)*	*p-value*
Ferritin (ng/mL)	246 (1054)	1360 (3668)	<0.001
D-dimer (ng/mL)	174 (903)	455 (1693)	0.0215
IL-6 (pg/mL)	2.97 (33.5)	8.54 (52.0)	0.141
Procalcitonin (ng/mL)	0.365 (3.56)	2.44 (10.8)	0.007
C-reactive protein (mg/L)	2.03 (4.62)	5.72 (8.56)	<0.001

Figure 3: Lymphocyte and eosinophil recovery associated with increased survival probability



Discussion

- COVID patients presenting with eosinopenia, neutrophilia, or lymphopenia have higher mortality rates
  - Eosinophils have been shown to demonstrate antigen presentation abilities along with upregulating costimulatory molecules CD40, CD80, and CD86 to enable CD4+ lymphocyte proliferation[1]
  - Eosinophils also express TLR7 which recognize ssRNA in viral particles[2]
- Although inflammatory markers are associated with severe COVID, only ferritin and C-reactive protein can reliably track disease progression
  - Possible limitation for assessing IL-6, D-dimer, and procalcitonin longitudinally is lack of lab testing during hospitalization
- Eosinophil and lymphocyte recovery lead to significantly better odds of survival
  - Previous studies have shown that recovered COVID patients who received convalescent plasma had restored NK and CD8+ T cells[3]

Future Directions:

- Multivariate analysis needed to consider confounding factors
- Eosinophil-lymphocyte axis may be area of further exploration as emerging evidence suggests that eosinophils have modulatory effects on T cell survival/proliferation

References

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3. Orologas-Stavrou, Nikolaos et al. "Peripheral Blood Immune Profiling of Convalescent Plasma Donors Reveals Alterations in Specific Immune Subpopulations Even at 2 Months Post SARS-CoV-2 Infection." *Viruses* 13.1 (2020): 26. *Crossref*. Web.

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