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Neutrophil-to-lymphocyte ratio and outcomes in Louisiana COVID-19 patients

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Abstract

Background: Due to the rapidly escalating number of cases and the low baseline of overall health in Louisiana, we sought to determine the prognostic value of the neutrophil-to-lymphocyte ratio (NLR) in hospitalized COVID patients in 2 major metropolitan areas with the highest prevalence of casesand exceedingly high rates of obesity and other comorbid conditions.We hypothesized that elevated NLR would be a prognostic indicator of mortality .

Methods: This was a review of a prospective registry of adult (18+ years) hospitalized SARS-CoV-2 patients from to two large urban safety net hospitals in Louisiana. Blood cell counts at days 2 and 5 were used to obtain NLR. Receiver operating characteristic (ROC) curve analysis assessed predictive capacity of NLR on mortality. Kaplan-Meier (KM) survival analysis and Cox regression models examined the effect of NLR on survival.

Results: The study population of 125 patients was majority African American (88.6%) and female (54.8%) with a mean age and BMI of 58.7 years and 34.2. Most (96.0%) had comorbiditiesof which hypertension (72.0%), obesity (66.7%), and diabetes (40.0%) were the most common. Mortality was 18.4%. NLR > 4.94 on day 1 predicted intubation ($P = 0.02$). NLR above established cutoff values on hospital days 2 and 5 each significantly predicted mortality ($P < 0.001$ and $P = 0.002$, respectively).

Conclusions:NLR is a prognostic factor for endotracheal intubation upon hospital admission and independent predictor for risk of mortality in SARS-CoV-2 patients on subsequent hospital days. Clinical research efforts should examine effects of strategies such as arginase inhibition alone and/or inhaled nitric oxide to ameliorate the effects of elevated NLR.

Keywords: neutrophil-to-lymphocyte ratio; coronavirus; inflammation; obesity; mortality

Introduction

In late 2019, a cluster of 27 cases of pneumonia caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), now commonly referred to as COVID-19,was discovered in the Hubei Province of China.(1) The first COVID-19 case was reported in the United States (US)in late January 2020, and in March, the World Health Organization officially classified the disease outbreak to be a pandemic.(2,3) As of April30, 2020, the United States (US) has surpassed all other countries in number of confirmed COVID-19 cases with over one million, more than ten times the reported numbers in China.(4) Several states have experienced larger, more severe outbreaks than others, with New York, New Jersey, and Louisiana being among the worst. Louisiana currently has more than 21,000 known cases, which is the 3rd highest number of cases per capita, and the fastest growth rate of coronavirus cases in the world.(5,6) That Louisiana has become a hotbed for COVID19 is not unexpected. In addition to the recent Mardi Gras celebrations which welcomed more than 1 million tourists to the state, Louisiana regularly ranks among the unhealthiest states in the nation.(7) In 2019, the state ranked 46th in cardiovascular deaths, 47th in diabetes, and 47th in obesity. In the same year, the state ranked last in health-related behavior, which included measures such as such as smoking (ranked 43rd), physical inactivity (ranked 46th), and high school graduation (ranked 47th).(7)

Inflammation plays a key role in the development of COVID-19 and is likely an important factor in its prognosis. The innate immune response to respiratory infection is characterized by an influx of neutrophils to the lungs, particularly the alveoli.(8) However, high levels of neutrophil infiltration may lead to collateral tissue damage, vascular stasis and cytotoxicity.(8-10) Previous studies have demonstrated that a sustained release of anti-inflammatory cytokines may lead to widespread apoptosis of lymphocytes, resulting in lymphopenia.(11-13)Specific to the current pandemic, high levels of circulating neutrophils have been demonstrated in COVID-19 patients, and a recently published meta-analysis of 660 total patients reported lymphopenia in over 40% of COVID-19 cases.(14,15)This imbalance of neutrophils to lymphocytes can be indicative of severe inflammatory progression, which could lead to the development ofsome of the significant complications so far observed in COVID-19 such as sepsis, multisystem organ dysfunction syndrome (MODS), and acute respiratory distress syndrome (ARDS).(14) Furthermore, levels of inflammatory mediators such as interleukin (IL)-6, C-reactive protein, and tumor necrosis factor alpha (TNFα) have been shown to be elevated in cases of obesity and obesity-related diseases.(16)

The neutrophil-to-lymphocyte ratio (NLR) has been identified as a marker of systemic inflammation and prognostic factor for mortality in several patient populations.(8,17-19)Due to the rapidly escalating number of cases and the low baseline of overall health in Louisiana, we sought to determine the prognostic value of the NLR in a population of COVID patients in the 2 major metropolitan areas with the highest prevalence of cases. These metropolitan areas are demographically similar, including similar poverty rates of 17%, and contain nearly half of the 4.6 million residents in the state. These areas are served by two, large safety net hospitals – both the only trauma centers in the region, which provided the patient population for the present study. We hypothesized that elevated NLR would be a prognostic indicator of mortality in a COVID-19 patient population.

Methods

This study was conducted following approval fromour Institutional Review Board. This was a review of a prospectively collected registry of adult (18+ years), hospitalized COVID-19 positive patients. Demographic and clinical data elements collected included: age, gender, comorbidities, daily lab values, initial vital signs upon presentation to the emergency department (ED), length of stay (LOS), intensive care unit LOS (ICU LOS), days utilizing mechanical ventilation, complete blood cell count and differential,and in-hospital mortality.Differentiated blood cell counts from hospital days 2 and 5 were used to calculate the neutrophil:lymphocyte ratio (NLR). Specifically, absolute neutrophil count was divided by absolute lymphocyte count toobtain the NLR for each hospital day examined. Patients were excluded if they were below 18 years of age or if they were still hospitalized and did not have recorded outcome data. Primary outcome of interest was in-hospital mortality. Secondary outcomes of interest were risk of intubation, length of stay, and mechanical ventilation days.

Statistical Analysis

Continuous variables were described as medians and interquartile ranges (IQR25 - IQR75), and categorical variables were described as frequencies and percentages. Differences in categorical values between groups were compared using Fisher's exact test or Chi Square analysis, while the Mann-Whitney U test was used to examine between group differences in continuous variables. Obesity was defined as body mass index (BMI) ≥ 30.0. Clinical diagnosis of complications were made using standard definitions such as Berlin criteria for ARDS and the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) score for renal failure.

Receiver operating characteristic (ROC) curve analysis was used to assess the predictive capacity of NLR on mortality. These results were reported as area under the curve (AUC) and 95% confidence intervals (CI). ROC curve analysis at hospital days 2 and 5 were used to establish NLR cut-off values by optimizing the Youden index.(20) Kaplan-Meier survival analysis was used to determine if these cut off values were predictive of in-hospital mortality.

Subjects who expired were censored at day of death. The log rank test was used to examine differences between survivors and expired subjects for each hospital day examined. Cox regression analysis was used to examine NLR at hospital days 2 and 5 as independent predictors of mortality, and its results were reported as Hazard Ratio (HR) and 95% CI. Significance was defined at the $P < 0.05$ level.

Results

A total of 188 patients were included in our institutionalCOVID-19 registry from two urban, safety net hospitals in southern Louisiana at the time of this analysis.(**Figure 1**) Of these, 125 had been discharged and recorded outcome data.The population was majority female (54.8%) with a mean (SD) age of 58.7 (14.8) years.(**Table I**) African American race comprised the majority (88.6%) of the patient population followed by white (4.9%). The most frequent chief complaints at presentation were shortness of breath (61.5%), fever (22.1%), and cough (15.4%). (**Table S1** http://links.lww.com/SHK/B66) Nearly all (95.7%) of the population presented with pre-existing comorbid conditions, of which hypertension (72.0%), obesity (66.7%), and diabetes mellitus (40.0%) were the most common.Overall mortality was 18.4%. There were no differences in mean age, mean body mass index (BMI), sex, race, smoking history, mean total comorbidities, or prevalence of any comorbidity between the alive and expired cohorts. Of the procedures performed in the ED that were examined, intubation and central line placement were both strongly associated with mortality ($P < 0.001$ for both). Mean hospital length of stay (LOS) was not different between survivors and decedents ($P = 0.127$). However, ICU LOS and days utilizing mechanical ventilation were each significantly longer in the expired patient subgroup ($P < 0.001$ for both). The overall complication rate was 47.1%; ARDS was the most commonly incurred complication and was recorded in 26.4% of the patient population. Renal failure was documented in 19.2% of patients, while sepsis was noted in 15.2%.

A ROC curve of the NLR at day 1 was created to determine if baseline NLR was predictive of intubation. (**Figure 2**) The area under the curve (AUC) for was 0.651 (95% CI 0.530 – 0.772, P = 0.002). A predictive cutoff value of 4.94 was established by maximizing Youden's index. Odds of intubation were significantly higher in those above the cutoff value compared to those below [Odds Ratio (OR) 1.148; 95% confidence interval (CI) 1.024 – 1.288; P = 0.014].

Table 2 details the cohort characteristics, admission vitals, and outcomes of the cohort with a baseline NLR above the cutoff value of 4.94 to those equal to or less than the cutoff. There were no differences observed in age, BMI, or ED vitals. Those above the established cutoff had significantly higher mean number of comorbid conditions than those below the cutoff (2.2 vs 2.6; P =0.013, respectively). A baseline NLR above the cutoff value was significantly associated with intubation at admission (P = 0.020). The elevated NLR cohort also had significantly longer mean ICU stays (2.6 days vs 1.1; P = 0.015) and more days utilizing mechanical ventilation (2.2 vs 0.9; P = 0.019) than did the cohort below the cutoff value. Renal failure occurred significantly more often in the higher NLR cohort (33.3% vs 8.1%, P = 0.001). Frequency of sepsis neared, but did not reach significance, and no differences were observed for the other complications examined.

In the ROC curve analysis for hospital day 2, the AUC for predicting in-hospital mortality by NLR was 0.713 (95% CI (0.564 - 0.862), *P* = 0.004)Sensitivity and specificity were 52.4% and 96.7%, respectively. For the NLR of hospital day 5, the AUC was 0.775 (95% CI (0.633 - 0.916), *P* = 0.002), sensitivity 52.9%, and specificity 93.8%. Analysis of the points of each ROC curve by maximizing Youden's index revealed optimal NLR cutoff values of 9.96 for hospital day 2 and 11.40for hospital day 5.

Kaplan-Meier survival curves were created using the established NLR cutoff points for hospital days 2 and 5. (**Figures 3A, B)** The differences in survival for COVID patients above the stated NLR cutoff value compared to those below the cutoff examined were highly statistically significant for each day examined (P< 0.001 for both). Cox regression analysis revealedNLR on day 2to be an independent predictor of in-hospital mortality (HR 1.07, 95% CI 1.029 – 1.108 - 4.202, P< 0.001). Similarly, on hospital day 5, NLR was found to be a strong prognostic factor for increased mortality (HR = 1.06, 95% CI 1.022 – 1.107, *P* = 0.002).

Discussion

The novel coronavirus, SARS-CoV-2, is a highly contagious and significantly fatal disease. At the time of this writing, there were more than 1.8 million known cases worldwide with a case fatality rate of 6.2%.(4) This fatality rate increases for cases severe enough to require hospitalization. Louisiana has one of the highest number of cases per capita numbering more than 20,000 total, of which approximately 10% (n = 2084) are hospitalized.(6)Many authors and news sources have hypothesized that the Mardi Gras holiday provided a fertile ground for the spread of COVID-19. As only 3 months have passed since the emergence of COVID-19, many clinical questions remain to be answered. Evidence-based treatments have yet to emerge, though many are in clinical trials. Protocols for when to intubate vary widely across institutions, likely a multifactorial result of resource-driven decision making and the heterogeneity of COVID patient presentation and clinical course.

The present study results maintain the previously demonstrated prognostic ability of the neutrophil to lymphocyte ratio in an unexplored patient population. This measure provides clinicians with a simple and easily obtainable tool to facilitate accurate prognostication in COVID-19 patients. Other known and well-established illness severity scoring systems and predictors of patient outcome such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) score are either too complex and cumbersome for regular use or are of little clinical utility in the acute phase. Conversely, the NLR adds no cost, is a simple and near real-time calculation using routine lab values, and can be employed as early as patient presentation, making NLR a practical and valuable clinical asset.

Patients with sustained, elevated NLR had worse results in almost all measured outcomes. An inflammatory response activates the local innate immunity of the body to provide protection against ingress of microorganisms. However, abnormalities can occur in host defense systems in response to infection. A dysregulated or unbalanced inflammatory response escalates and releases an excess of pro-inflammatory mediators such as IL-1, IL-6, IL-8, and TNFα, which can results in systemic inflammatory response syndrome (SIRS).(21,22) Progression of this cascade and hyper-inflammation worsens the initial burden. High levels of neutrophil infiltration and systemic circulation result in increased systemic arginase activity, which results in depleted systemic arginine.(23,24) Arginine is the sole substrate for nitric oxide (NO) production, which has known anti-viral activity against RNA viruses such as SARS-CoV-2.(23,25,26)Concurrent with impaired NO production due to depletion of arginine, lymphocytes succumb to environmental stress and are lost to cytokine-induced apoptosis. This systemic dysregulation of the immune system, particularly in the setting of inflammatory comorbid conditions such as obesity and obesity-related diseases, can manifest as deleterious and often life-threatening events such sepsis and MODS.(27,28) Prevalence of these outcomes were higher in patients with an elevated NLR at admission. Overall rate of ARDS was 26.4%, in line with previous reports of 19% - 29.3%, but occurred in 35.1% of patients with NLR > 4.94 at admission.(15,29)Similarly, sepsis and MODS were found to occur in 15.2% and 2.4%, respectively of the study population, but were documented in 22.8% and 5.3% of patients with an elevated baseline NLR. These results indicate that the neutrophil to lymphocyte ratio has potential utility as an early indicator of inflammatory derailment in COVID-19 patients.

A striking finding in this study is the high proportion of patients that were African American. While this finding has been reported in other locales across the United States, the disparities that exist in Louisiana are profound. Approximately 33% of the population of Louisiana is African American. In the New Orleans and Baton Rouge metropolitan areas, African Americans comprise 60.2% and 47.0% of the population, respectively.(30) Yet this demographic comprised an alarming 88.6% of the present study population. This disparity in the COVID-19 patient population may be, at least partly, explained by a lower baseline of health in the African American community compared to their white counterparts. According to a 2018 report 43.5% of black adults in Louisiana are obese compared to 32.9% of whites.(31) Obesity was also more common in women (39.5%) than men (34.1%), which may help to explain the larger proportion of women than men in our present study. A previous report analyzed the National Health and Nutrition Examination Survey (NHANES) to investigate differences of NLR values in the general population and across race.(32) Interestingly, it was reported that non-Hispanic black and Hispanic subjects had significantly lower mean NLR values. Subjects with comorbidities such as diabetes, obesity, and cardiovascular disease had significantly higher NLR than those not burdened with comorbidities.(32) The same study also found that black/African

American population with diabetes had significantly higher NLR compared to their non-diabetic counterparts. Taken together, the higher prevalence of obesity and diabetes in Louisiana in general, but in the African American community especially, and the high poverty rateswithin that community that may adversely impact access to care, may offer insight into the racial disproportionality observed in the present study. Furthermore, despite being reported to have lower baseline NLR compared to whites, the high level of pre-existing conditions may have reversed this difference, resulting in increased severity of illness in African American patients. Our study was unable to determine racial differences in NLR due to the overwhelming majority being African American.

The prevalence of comorbidities in this study was 96%. This numbervastly exceeds previous reports in other COVID-19 patient populations.(29,33,34)In a recent publication by the Center for Disease Control and Prevention (CDC), underlying health conditions were reported in 37.6% of 122,653 American COVID-19 patients.(34)Several recent reports have demonstrated that the presence of hypertension, diabetes, respiratory disease, and cardiovascular disease each increased the risk of progression to severe illness in this novel coronavirus.(33) All of these conditions are more prevalent in the presence of obesity, which was observed in nearly 67% of the present study population.Diabetics have a higher overall risk of infection that results from multiple perturbations of innate immunity which include impaired phagocytosis by neutrophils, macrophages and monocytes, impaired neutrophil chemotaxis and bactericidal activity, and impaired innate cell-mediated immunity.(35) People with diabetes also have a low-grade chronic inflammation which might facilitate the cytokine storms that may be the cause of the severe cases of pulmonary disease seen with COVID-19 and of the eventual death of many patients. Additionally, higher glucose levels and pre-existing diabetes were independent risk factors for morbidity and mortality in patients with the original SARS outbreak in 2003.(36)Our results support the idea that pre-existing, chronic inflammation contributes to increased severity of disease and poor outcomes in SARS-CoV-2 cases. Here, the elevated NLR subgroup on day of hospital admission had a higher mean number of comorbidities, which likely explains theheightened degree of inflammation observed compared to those with a lower burden of pre-existing disease. A combination of higher baseline inflammation withimmune-mediated inflammation due to SARS-CoV-2 infection maycontribute to systemic dysregulation of the immune system, and may, at least partially, explain the poor outcomes observed in the elevated NLR group, including increased risk of intubation on hospital day 1, longer ICU stays, and longer time utilizing mechanical ventilation. Together, these previous and present findings lend support to recent statements that low baseline health is a primary driver in the high number of critical and fatal cases in south Louisiana.

Study Limitations

The present study possesses several limitations. The cut points in this analysis were derived from the same data set utilized for the NLR-related survival analysis. A cross-validation of a "hold-out" sample would have strengthened our findings; however, the sample size available was not of sufficient size to conduct such an analysis. It may remain necessary to conduct an external validation of the presented findings. Despite this, the present results are in line with the previously demonstrated prognostic ability of the NLR and in a previously unstudied patient population. Therefore, we believe that the trends and predictors demonstrated here are likely real while realizing that external validation would strengthen our conclusions. Additionally, despite existing institutional protocols, the criteria utilized to inform intubation of patients has changed and continues to change as a result of resource limitations. This may represent a source of bias in this patient cohort.

Conclusions

NLR has marked potential to be a prognostic factor for endotracheal intubation on the initial day of hospital admission and as a powerful predictor for risk of mortality in COVID-19 patients on subsequent hospital days. Clinical research efforts should examine strategiesto ameliorate the effects of elevated NLR in this at-risk population in order to improve treatment and reduce mortality.

AUTHOR CONTRIBUTION

Study conception and design:

Tatum, Duchesne

Acquisition of data:

Houghton, Tatum, Stover, Toraih

Analysis and interpretation of data:

Tatum, Toraih, Taghavi, Duchesne

Drafting of manuscript:

Tatum, Taghavi

Critical revision:

Tatum, Taghavi, Houghton, Toraih, Stover, Duchesne

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FIGURE LEGEND

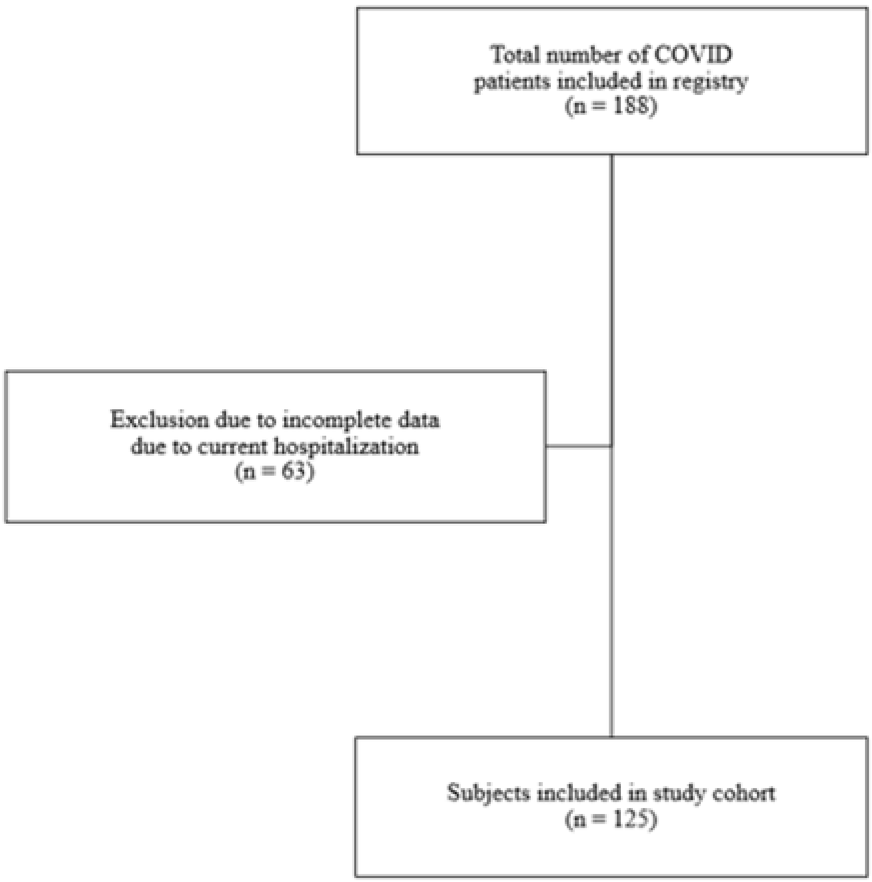


Figure 1. Flow diagram for study inclusion

Figure 2. Receiver operating characteristic (ROC)curve of NLR on hospital day 1 predicting intubation

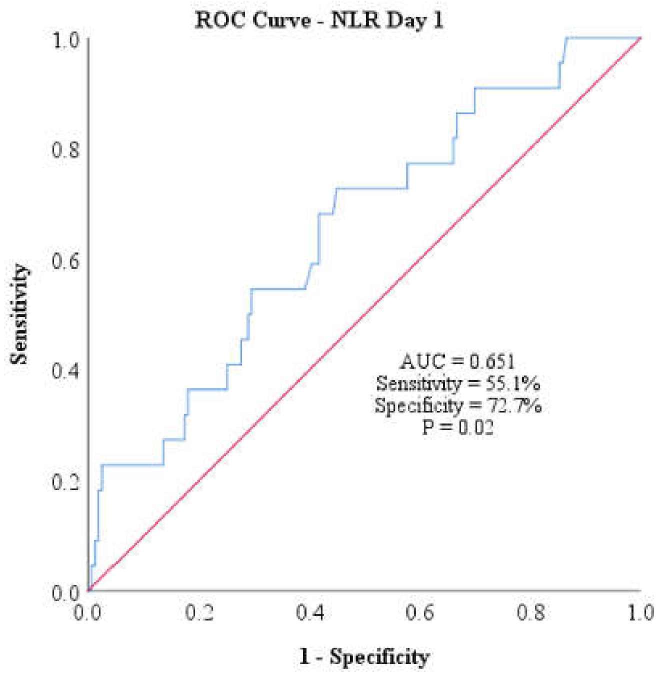
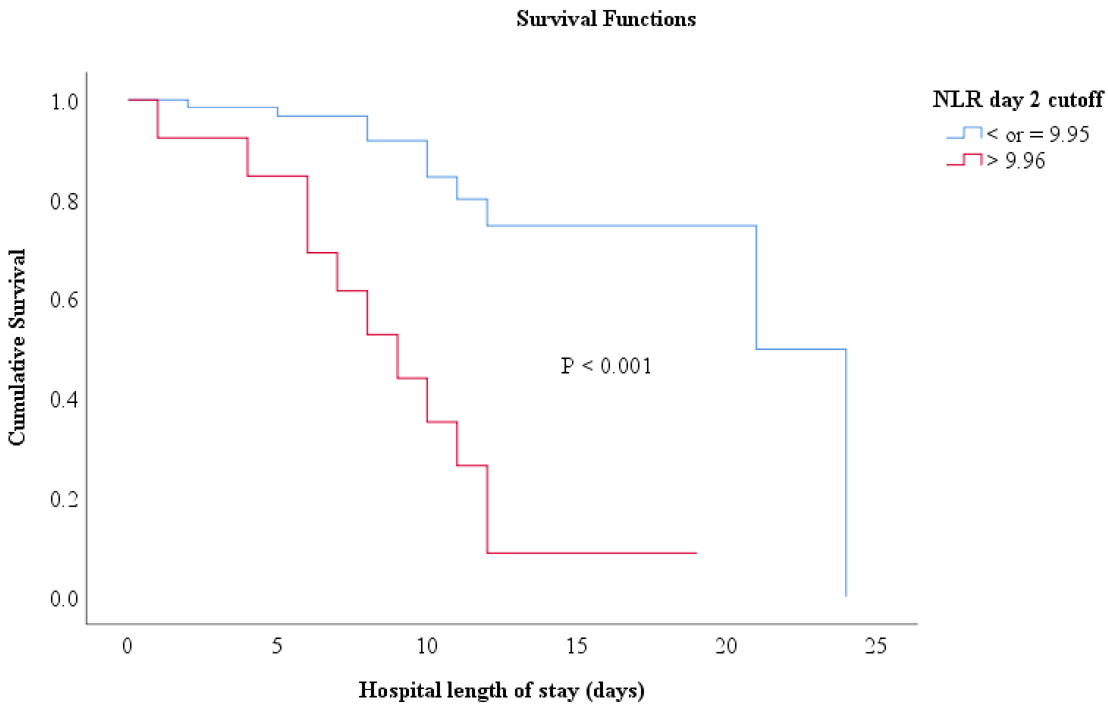


Figure 3. Kaplan-Meier survival curves of hospitalized COVID-19 patients above and below established neutrophil to lymphocyte ratio (NLR) cutoff values on **(A)**hospital day 2and **(B)** hospital day 5.

A.



B.

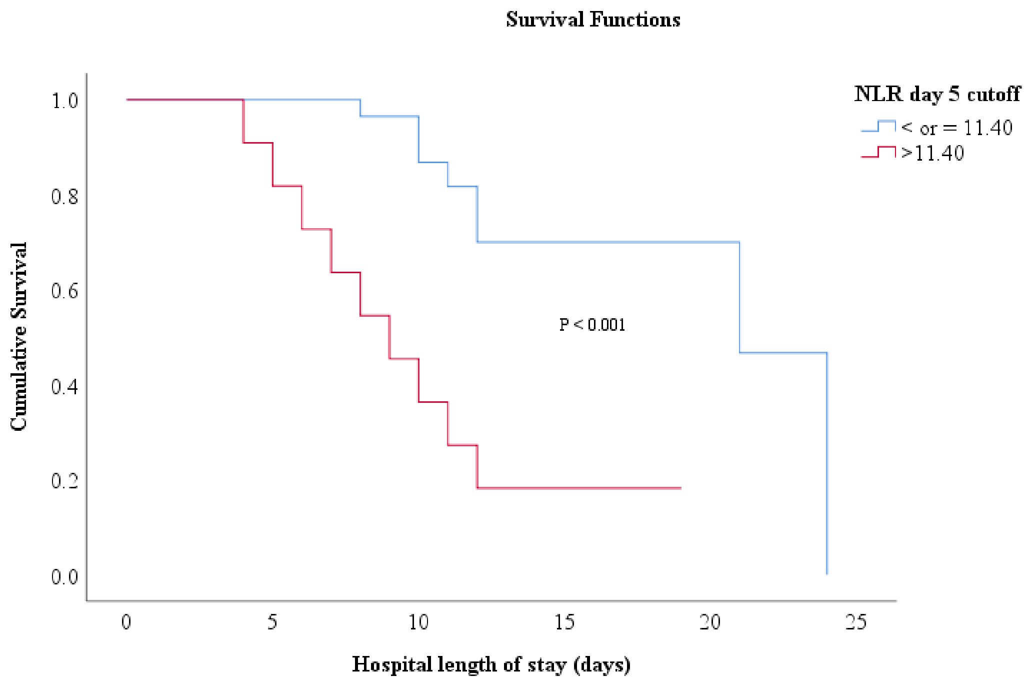

Survival Functions
NLR day 5 cutoff
< or = 11.40
>11.40
P < 0.001
1.0
0.8
0.6
0.4
0.2
0.0
Cumulative Survival
0
5
10
15
20
25
Hospital length of stay (days)

Table 1. Patient demographics, clinical presentation, and in-hospital outcomes of COVID-19 patients.

Descriptor	Total (n = 125)	Alive (n = 102)	Expired (n = 23)	P
Age (years), mean (SD)	58.7 (14.8)	55.9 (15.4)	62.5 (12.7)	0.060
BMI, mean (SD)	34.2 (9.1)	33.6 (8.8)	36.6 (9.0)	0.148
Female Sex	68 (54.8)	57 (56.4)	11 (47.8)	0.454
Race				
Caucasian	6 (4.9)	6 (6.0)	0	0.199
Black/AA	109 (88.6)	88 (88.0)	21 (91.3)	
Asian/Unknown	7 (5.6)	5 (6.0)	2 (8.6)	
Not Hispanic or Latino ethnicity	118 (95.9)	96 (96.0)	22 (95.7)	0.643
Comorbidities (Y/N)	120 (96.0)	98 (96.1)	22 (95.7)	0.925
Total comorbidities, mean (SD)	2.3 (1.4)	2.3 (1.5)	2.7 (1.5)	0.216
ED vitals, mean (SD)				
Temperature (°C)	40.8 (12.7)	39.2 (8.4)	43.9 (18.7)	0.071
Heart rate (beats/minute)	98 (23)	95 (20)	97 (17)	0.651
SBP (mmHg)	136 (76)	129 (19)	142 (23)	0.006
RR (breaths/minute)	24 (7)	23 (6)	27 (8)	0.033
ED procedures				
Oxygen therapy (not including ventilation)	66 (52.8)	56 (54.9)	10 (43.5)	0.322
Intubation	16 (12.8)	3 (2.9)	13 (56.5)	< 0.001
Central line placement	3 (2.4)	0	3 (13.0)	< 0.001
IV access	107 (85.6)	88 (86.3)	19 (82.6)	0.651
Foley catheter	8 (6.4)	4 (3.9)	4 (17.4)	0.017
ICU admission from ED	21 (16.9)	8 (78)	13 (59.1)	< 0.001
Outcomes				
LOS (days), mean (SD)	7.6 (4.7)	7.2 (4.5)	9.3 (5.2)	0.058
ICU LOS, mean (SD)	1.8 (3.3)	0.6 (1.6)	6.8 (3.9)	< 0.001
ICU-free days, mean (SD)	6.0 (4.4)	7.0 (4.2)	1.9 (2.9)	< 0.001
Ventilator days, mean (SD)	1.4 (3.0)	0.3 (1.1)	6.2 (3.6)	< 0.001
Ventilator-free days, mean (SD)	6.2 (4.5)	7.2 (4.2)	2.3 (3.2)	< 0.001
Complications				
None	61 (48.8)	61 (59.8)	0	< 0.001
Renal failure	24 (19.2)	9 (8.8)	15 (65.2)	< 0.001
ARDS	33 (26.4)	17 (16.7)	16 (69.6)	< 0.001
MODS	3 (2.4)	0	3 (13.0)	< 0.001
Unplanned reintubation	6 (4.8)	1 (1.0)	5 (21.7)	< 0.001
Sepsis	19 (15.2)	10 (9.8)	9 (39.1)	< 0.001

Values are frequencies reported as n (%) unless otherwise noted. SD – standard deviation; ED – emergency department; C – Celsius; SBP – systolic blood pressure;RR – respiratory rate. IV – intravenous; ICU – intensive care unit;LOS – length of stay; ARDS – acute respiratory distress syndrome; MODS – multisystem organ dysfunction syndrome

Table 2. Descriptors and outcomes of COVID-19 patients above and below NLR day 1 cutoff value

Descriptor	NLR day 1 ≤ 4.94 (n =62)	NLR day 1 > 4.94 (n = 57)	P
Age, mean (SD)	56.1 (15.2)	62.1 (14.1)	0.007
BMI, mean (SD)	35.4 (9.5)	32.3 (8.3)	0.074
Female sex	35 (57.4)	30 (52.6)	0.605
# of comorbidities	2.2 (1.3)	2.6 (1.6)	0.013
ED vitals			
Temperature (°C)	41.4 (14.1)	40.3 (11.3)	0.576
HR (beats/minute)	97 (20)	99 (20)	0.571
SBP (mmHg)	138 (106)	133 (20)	0.706
RR (breaths/minute)	23 (6)	25 (7)	0.250
ED procedures			
Oxygen therapy (not including ventilator)	29 (46.8)	34 (59.6)	0.160
Intubation	4 (6.5)	12 (21.1)	0.020
Central line placement	0	3 (5.3)	0.067
IV access	54 (87.1)	50 (87.7)	0.919
Foley catheter	3 (4.8)	5 (8.8)	0.392
Outcomes			
LOS (days), mean (SD)	7.6 (5.0)	7.9 (4.3)	0.743
ICU LOS, mean (SD)	1.1 (2.7)	2.6 (3.8)	0.015
ICU-free days, mean (SD)	6.8 (4.1)	5.3 (4.7)	0.076
Ventilator days, mean (SD)	0.9 (2.3)	2.2 (3.5)	0.019
Ventilator-free days, mean (SD)	6.8 (4.3)	5.7 (4.7)	0.206
Complications			
Renal failure	5 (8.1)	19 (33.3)	0.001
ARDS	13 (21.0)	20 (35.1)	0.086
MODS	0	3 (5.3)	0.067
Unplanned reintubation	3 (4.8)	3 (5.3)	0.916
Sepsis	6 (9.7)	13 (22.8)	0.051
Death	9 (14.3)	14 (24.6)	0.153

Values are frequencies reported as n (%) unless otherwise denoted. NLR – neutrophil to lymphocyte ratio; SD – standard deviation; BMI – body mass index; ED – emergency department; C – Celsius; IV – intravenous; HR – heart rate; SBP – systolic blood pressure; RR – respiratory rate; LOS – length of stay; ICU – intensive care unit; ARDS – acute respiratory distress syndrome; MODS - multisystem organ dysfunction syndrome