

Brief Report

Prognostic Performance of Inflammatory Biomarkers Based on Complete Blood Counts in COVID-19 Patients

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Abstract: With the end of the pandemic, COVID-19 has entered an endemic phase with expected seasonal spikes. Consequently, the implementation of easily accessible prognostic biomarkers for patients with COVID-19 remains an important area of research. In this monocentric study at a German tertiary care hospital, we determined the prognostic performance of different clinical and blood-based parameters in 412 COVID-19 patients. We evaluated the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), pan-immune-inflammation value (PIV), and absolute eosinopenia (AEP, 0/ μ L) of COVID-19 patients ($n = 412$). The Siddiqui and Mehra staging proposal, the WHO clinical progression scale, and COVID-19-associated death were used as COVID-19 outcome measures. With respect to Siddiqui and Mehra staging, patient age of older than 75 years, high C-reactive protein (CRP), absolute eosinopenia (AEP), cardiovascular comorbidities, and high ferritin were significant independent predictors for severe COVID-19. When outcome was determined according to the WHO clinical progression scale, patient age of older than 75 years, high CRP, high LDH, AEP, high neutrophil-to-lymphocyte ratio (NLR), and the presence of pulmonary comorbidities were significant independent predictors for severe COVID-19. Finally, COVID-19-associated death was predicted independently by patient age of older than 75 years, high LDH, high NLR, and AEP. Eosinopenia ($< 40/\mu$ L) was observed in 74.5% of patients, and AEP in almost 45%. In conclusion, the present real-world data indicate that the NLR is superior to more complex systemic immune-inflammation biomarkers (e.g., SII and PIV) in COVID-19 prognostication. A decreased eosinophil count emerged as a potential hallmark of COVID-19 infection, whereas AEP turned out to be an accessible independent biomarker for COVID-19 severity and mortality.

Keywords: SARS-CoV-2; eosinophils; eosinopenia; systemic immune-inflammation; C-reactive protein; lactate dehydrogenase; ferritin; comorbidities



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1. Introduction

In May 2023, the World Health Organization (WHO) declared an end to the public health emergency related to coronavirus disease 2019 (COVID-19). At that time, 765 million confirmed cases and about 7 million deaths had been reported worldwide. As COVID-19 has entered an endemic phase, seasonal spikes may still inflict significant stresses

on national health systems. Therefore, the implementation of prognostic markers for risk stratification, the optimization of hospitalization rates, and the monitoring of COVID-19 patients remains an important area of research [1–5].

Clinical features, including age and age-related comorbidities (such as lung disorders, cardiovascular disease, and diabetes mellitus) as well as elevated laboratory parameters (C-reactive protein, ferritin, D-dimer, lactate dehydrogenase, lymphocytes) have been established as consistent predictors of severe COVID-19 associated with pneumonia, subsequent immediate care unit admission, and a fatal outcome [1–3,6,7]. Moreover, a variety of systemic immune-inflammation biomarkers based on complete blood counts (CBCs), including the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII), have shown prognostic potential in COVID-19 [6,7]. However, the relatively new and more complex pan-immune-inflammation value (PIV) has not yet been studied in COVID-19. Apart from neutrophils, lymphocytes, and platelets, the PIV also includes monocytes in its formula, which have also been shown to be involved in COVID-19 progression. Blood eosinophils have received less attention in this context than the aforementioned prognostic factors such as NLR. Whereas eosinophil count was not considered a prognostic biomarker at the beginning of the pandemic [8], evidence has now accumulated showing that eosinophil count might help to differentiate COVID-19 infection from other lung conditions, and additionally serve as a predictor of disease severity [9–11]. Here, we conducted a comprehensive retrospective/prospective study comparing a large panel of clinical and laboratory parameters including absolute eosinophil counts and the PIV in a German cohort of patients infected with SARS-CoV-2. Data were then correlated with three different outcome measures.

2. Materials and Methods

2.1. Patients

This retrospective/prospective study consecutively recruited COVID-19 patients from the beginning of 2020 to the end of 2021 at a tertiary care hospital (St. Josef) of the Ruhr-University Bochum (Bochum, Germany). Laboratory-confirmed COVID-19 patients with CBCs performed on admission were included in the study (ethics approval: #20-6953-bio). SARS-CoV-2 detection was carried out using a commercial qPCR assay on nasopharyngeal swab specimens (Allplex™ 2019-nCoV, Seegene, South Korea) according to standard protocols. Pregnant females, children (age < 16 years), those with a condition affecting laboratory parameters (including metastatic cancer or chronic haematological conditions), those who had received corticosteroid medication on admission, and those whose outcome was unknown were excluded from this investigation (Figure 1). A healthy sex/age-matched control group ($n = 29$) was also studied with respect to the CBC-based systemic immune-inflammation biomarkers PIV, SII, and NLR.

2.2. Data Extraction and Outcome Measures

All data were extracted from electronic medical files. These data included patient characteristics, comorbidities, length of in-patient treatment, treatment details, laboratory data, and clinical outcomes. More details are provided in Tables 1 and 2. COVID-19 progression and the final disease outcome of COVID-19 were evaluated using three metrics. First, clinical-therapeutic staging, as proposed by Siddiqi and Mehra: I = early infection; IIA = pulmonary involvement without hypoxia; IIB = pulmonary involvement with hypoxia; and III = systemic hyperinflammation [12]. Second, the WHO clinical progression scale, which provides a measure of illness severity across a range from 0 (not infected) to 10 (dead) and groups these in stages: I = score 1–3; II = score 4 and 5; III = score 6–9; and IV = score 10 [13]. As a third measure of outcome, COVID-19-associated death was included. For statistical analysis, we dichotomized clinical-therapeutic staging by grouping stages I and IIA vs. IIB and III, and the WHO clinical progression scale by grouping stages I and II vs. III and IV. Importantly, all outcome measures were based on data easily extracted from standard electronic medical files.

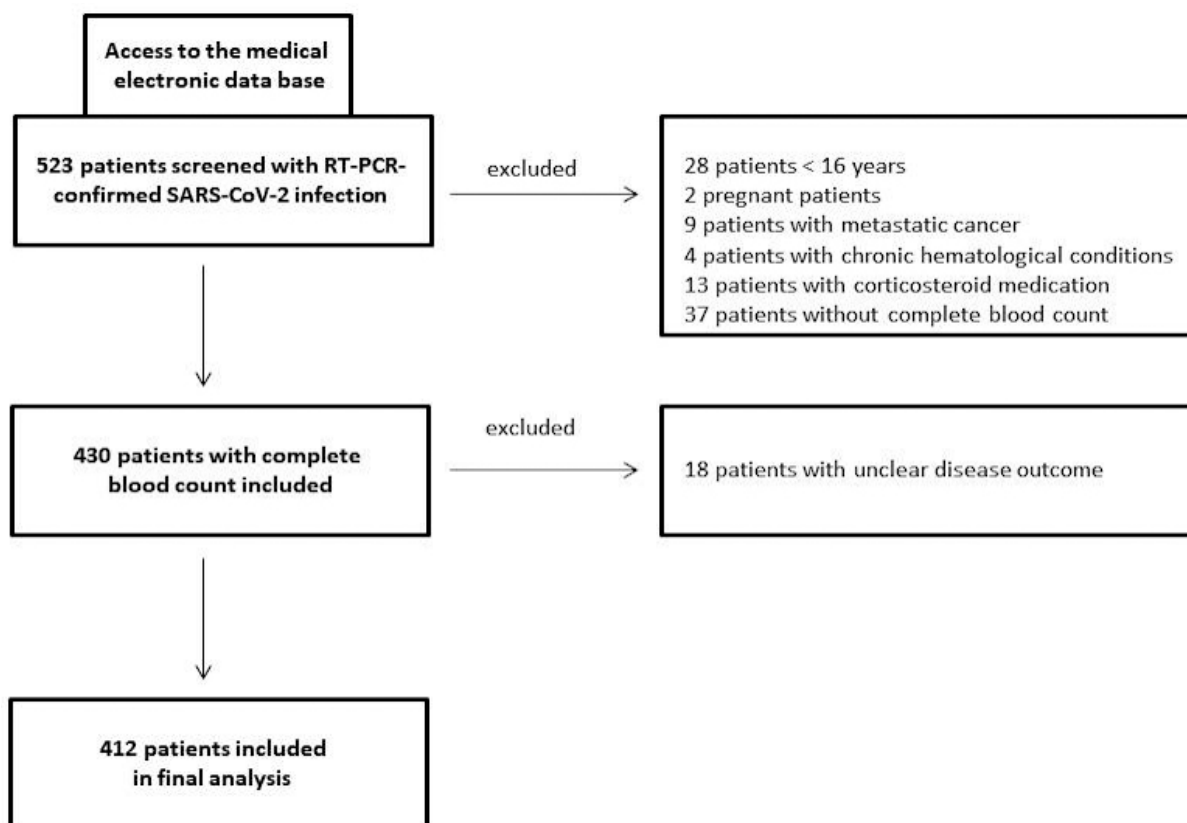


Figure 1. Study flow chart of COVID-19 patients investigated in a German tertiary care hospital from the beginning of 2020 to the end of 2021.

2.3. Laboratory Tests

Parameters based on CBCs included absolute neutrophils, lymphocytes, monocytes, eosinophils, and thrombocytes. Systemic immune-inflammation biomarkers included the PIV, which was calculated from absolute values as follows: neutrophils/ μL \times platelets/ μL by lymphocytes/ μL \times monocytes/ μL by lymphocytes/ μL [14,15]. The SII was calculated using the following formula: neutrophils/ μL \times platelets/ μL by lymphocytes/ μL . Using absolute blood count values, we also determined the NLR by dividing neutrophils/ μL by lymphocytes/ μL . Absolute eosinopenia (AEP) was defined as eosinophil count = 0/ μL [10,11]. Moreover, we assessed levels of serum C-reactive protein (CRP), ferritin, and lactate dehydrogenase (LDH).

2.4. Statistics

For statistical analysis, MedCalc (Ostende, Belgium) software version 20.009 was used. Analysis of data distribution was performed using the D'Agostino–Pearson test. Univariable statistics included the χ^2 test for dichotomized data and receiver operating characteristics (ROC) analyses for continuous data [including associated criterion, area under the curve (AUC), and Youden index (optimal cut-off points of both the maximum sensitivity and specificity)]. Multivariable testing was performed using logistic regression and only included data with significance from univariate testing, specifically an AUC of ≥ 0.70 on ROC analysis or significance with χ^2 analysis. As required, variables included for testing independence did not strongly correlate with each other. Odds ratios (OR) including the 95% confidence intervals (CI) were calculated as well; $p < 0.05$ was considered statistically significant.

Table 1. Descriptive clinical baseline data of COVID-19 patients ($n = 412$) treated in a German tertiary care hospital (a). Comorbidities and course of COVID-19 are shown in part (b).

(a)		(b)	
Parameter	Data	Parameter	Data
Sex		Obesity	
Female/male	199/213 (48.3%/51.7%)	no/yes	324/88 (78.6%/21.4%)
Median age (years)	58 (16–97)	Diabetes mellitus	
Body mass index (kg/m ²)	27.7 (17.3–50.5)	no/yes	314/97 (76.4%/23.6%)
Vaccination status		Smoking	
No vaccination	367 (89.1%)	no/yes	359/53 (87.1%/12.9%)
1st vaccination	19 (4.6%)	Lung diseases	
2nd vaccination	23 (5.6%)	no/yes	338/74 (82%/18%)
1st booster	3 (0.7%)	Cardiovascular diseases	
2nd booster	0 (0%)	no/yes	189/223 (45.9%/54.1%)
Recovery rate		Neuropsychiatric diseases	
no/yes	409/3 (99.3%/0.7%)	no/yes	328/84 (79.6%/20.8%)
Median Ct-value		At least two comorbidities	
(S-gene)	22 (7–38)	no/yes	198/214 (48.1%/51.9%)
(E-gene)	23 (10–37)	Staging by Siddiqi and Mehra	
(RdRP-gene)	24 (7–39)	Stage I	89 (21.6%)
(N-gene)	25 (11–287)	Stage IIA	52 (12.6%)
Fever (≥ 38 °C)		Stage IIB	223 (54.1%)
no/yes	319/79 (80.2%/19.8%)	Stage III	49 (11.9%)
Dysnosomie		WHO clinical progression scale	
no/yes	326/86 (79.1%/20.9%)	I	93 (22.6%)
Breathing rate		II	211 (51.2%)
median	19 (8–50)	III	54 (13.1%)
Oxygen saturation		IV	55 (13.3%)
median percentage	97 (40–100)	COVID-19 pneumonia	
Days with symptoms before admission		no/yes	104/307 (25.3%/74.7%)
median	6 (1–22)	Intensive care unit (ICU)	
In-patient treatment		no/yes	312/100 (75.7%/24.3%)
no/yes	23/389 (5.6%/94.4%)	median days on ICU	9.5 (1–85)
Duration of in-patient treatment		Deceased with COVID-19	
median	10 (1–194)	no/yes	357/55 (86.7%/13.3%)
		Duration of in-patient treatment	
		median	10 (1–194)
		Breathing support	
		no	140 (34%)
		oxygen via nasal canula	179 (43.4%)
		high-flow oxygen, non-invasive ventilation	56 (13.6%)
		intubation	26 (6.3%)
		ECMO	11 (2.6%)
		Anti-COVID-19 therapy	
		no	216 (52.4%)
		dexamethasone	97 (23.5%)
		remdesivir	31 (7.5%)
		dexamethasone/remdesivir	48 (11.7%)
		miscellaneous	20 (4.9%)

Table 2. Baseline laboratory data including systemic immune-inflammation markers of COVID-19 patients treated in a German tertiary care hospital.

Parameter	Data
C-reactive protein (mg/L)	
median (range)	36.3 (1–558)
Lactate dehydrogenase (U/L)	
median (range)	261.5 (86–1156)
Ferritin (ng/mL)	
median (range)	409 (5–10,627)
Neutrophils (/μL)	
median (range)	3955 (900–18,200)
Lymphocytes (/μL)	
median (range)	1090 (240–5090)
Monocytes (/μL)	
median (range)	440 (70–7300)
Eosinophils (/μL)	
median (range)	10 (0–480)
Eosinopenia (<40/μL)	
no/yes	105/307 (25.5%/74.5%)
Absolute eosinopenia (0/μL)	
no/yes	228/184 (55.3%/44.7%)
Thrombocytes (/μL)	
median (range)	189,000 (24,000–784,000)
Neutrophil-to-lymphocyte ratio	
median (range)	3.7 (0.55–72.6)
healthy controls	1.9 (0.9–11.6) $p < 0.0001$
Systemic immune-inflammation index	
median (range)	688 (39.7–14,661)
healthy controls	425 (39.3–5946) $p = 0.0002$
Pan-immune-inflammation value	
median (range)	288 (16.8–24,338)
healthy controls	275 (81–1621) $p = 0.47$

3. Results

3.1. Patient Characteristics and Outcome Measures

A total of 412 qPCR-confirmed COVID-19 patients were included in this study (199 females and 213 males). The median age was 58 years (range: 16–97 years, Table 1). In this cohort, 367 patients were not vaccinated (89.1%). At least two comorbidities were observed in 214 patients (51.9%). Almost all patients (389, 94.4%) were hospitalized, with a median stay of 10 days (range: 1–194). Laboratory parameters obtained on admission are detailed in Table 2. AEP was observed in 184 patients (44.7%). According to clinical-therapeutic staging as proposed by Siddiqi and Mehra, 271 patients had more severe disease (65.8%, Table 1b). By contrast, according to the WHO clinical classification scale, 108 patients were grouped as having more severe COVID-19 (26.2%).

In this cohort, 100 patients required treatment in the intensive care unit (ICU) with a median stay of 10 days (24.3%, range 1–85). Ventilation support of any kind was observed in 272 patients (66%). COVID-19-associated death was observed in 55 patients (13.3%).

3.2. Univariable Analysis

A comparison with healthy controls revealed that the NLR ($p < 0.0001$) and SII ($p = 0.0002$), but not the PIV ($p = 0.47$), were significantly higher in COVID-19 patients (Table 3). Moreover, PIV failed to reach an $AUC \geq 0.70$ on ROC analysis for each of the three outcome measures studied. Univariable analyses are shown in Table 3, including all significant parameters for χ^2 test analysis and significant parameters for ROC analysis with an $AUC \geq 0.70$.

Table 3. Univariable analysis including receiver operating curves (ROC) and χ^2 tests in order to determine significant prognostic biomarkers for the outcome of patients with COVID-19. We exclusively included parameters revealing a significant $AUC \geq 0.70$ on ROC analysis or a statistically significant result on χ^2 test.

Parameter	Prognostic for Class IIB and III (Siddiqi and Mehra) [12]	Prognostic for Class III and IV (WHO) [13]	Prognostic for COVID-19 Death
Ferritin	AUC 0.77, $p < 0.0001$ Criterion: >465 , Youden index: 0.41	-	-
LDH	AUC 0.81, $p < 0.0001$ Criterion: >239 , Youden index: 0.50	AUC 0.78, $p < 0.0001$ Criterion: >371 , Youden index: 0.41	AUC 0.78, $p < 0.0001$ Criterion: >339 , Youden index: 0.45
C-reactive protein	AUC 0.85, $p < 0.0001$ Criterion: >26 , Youden index: 0.54	AUC 0.81, $p < 0.0001$ Criterion: >83 , Youden index: 0.47	AUC 0.79, $p < 0.0001$ Criterion: >47 , Youden index: 0.46
Age > 75 years	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$
Diabetes	$p = 0.014$	-	$p < 0.0001$
Obesity	-	$p = 0.0047$	-
Cardiovascular diseases	$p < 0.0001$	$p = 0.0004$	$p < 0.0001$
Lung diseases	$p = 0.006$	$p < 0.0001$	$p = 0.0073$
Two or more comorbidities	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$
Absolute eosinopenia	$p < 0.0001$	$p < 0.0001$	$p < 0.0001$
NLR	-	AUC 0.72, $p < 0.0001$ Criterion: >5.4 , Youden index: 0.32	AUC 0.74, $p < 0.0001$ Criterion: >7.4 , Youden index: 0.47
SII	-	-	AUC 0.70, $p < 0.0001$ Criterion: >1196 , Youden index: 0.37

Significant predictors for severe disease (stages IIB and III) according to clinical-therapeutic staging as proposed by Siddiqi and Mehra included high ferritin, LDH, CRP, a patient age of above 75 years, AEP, and comorbidities, including cardiovascular diseases, lung diseases, diabetes mellitus, and the presence of two or more comorbidities (Table 3). Significant predictors for severe disease (classes III and IV) according to the WHO clinical classification scale included high LDH, CRP, age, AEP, and NLR, and comorbidities, including cardiovascular diseases, lung diseases, and obesity, and the presence of two or more comorbidities (Table 3). COVID-19-associated death was significantly associated with AEP, high LDH and CRP, age, systemic immune-inflammation biomarkers such as NLR and SII, and comorbidities, including cardiovascular diseases, lung diseases, and diabetes mellitus, and the presence of two or more comorbidities.

3.3. Multivariable Analyses

Using clinical-therapeutic staging as proposed by Siddiqi and Mehra for multivariate analysis, the following parameters emerged as independent predictors of severe disease (stages IIB and III): age greater than 75 years (OR 2.3, 95% CI 1.1 to 4.7, $p = 0.021$), high CRP (OR 4.5, 95% CI 2.2 to 9, $p < 0.0001$), AEP (OR 4.4, 95% CI 2.4 to 7.6, $p < 0.0001$), absence of cardiovascular comorbidities (OR 0.43, 95% CI 0.20 to 0.88, $p = 0.022$), and high ferritin (OR 1.0006, 95% CI 1.0001 to 1.0012, $p = 0.026$, Table 4).

Table 4. Multivariable analyses (logistic regression models) included dependent variables such as COVID-19-associated death and class 2 and 3 classifications according to the Siddiqi and Mehra classification and WHO clinical progression scale [12,13]. Independent variables were included in the model if there was a significant AUC ≥ 0.70 on ROC analysis or a statistically significant result on Chi² testing for dichotomous variables.

Parameter	Prognostic for Class IIB and III (Siddiqi and Mehra) [12]	Prognostic for Class III and IV (WHO) [13]	Prognostic for COVID-19 Death
Ferritin	OR 1.0006, 95% CI 1.0001 to 1.0012, $p = 0.026$	-	-
LDH	-	OR 2.7, 95% CI 1.4 to 5.0, $p = 0.027$	OR 4.2, 95% CI 1.8 to 10, $p = 0.0012$
C-reactive protein	OR 4.5, 95% CI 2.2 to 9, $p < 0.0001$	OR 4.4, 95% CI 2.4 to 7.6, $p < 0.0001$	-
Age	OR 2.3, 95% CI 1.1 to 4.7, $p = 0.021$	OR 2.3, 95% CI 1.2 to 4.4, $p = 0.011$	OR 8.3, 95% CI 3.5 to 19.8, $p < 0.0001$
Absence of cardiovascular diseases	OR 0.43, 95% CI 0.20 to 0.88, $p = 0.022$	-	-
Lung diseases	-	OR 2.3, 95% CI 1.1 to 4.6, $p = 0.013$	-
Absolute eosinopenia	OR 4.4, 95% CI 2.4 to 7.6, $p < 0.0001$	OR 3.2, 95% CI 1.8 to 5.6, $p = 0.0001$	OR 2.6, 95% CI 1.2 to 5.7, $p = 0.017$
NLR	-	OR 2.5, 95% CI 1.3 to 4.9, $p = 0.006$	OR 2.8, 95% CI 2.1.1 to 7.4, $p = 0.035$

When the WHO clinical classification system was used as an outcome measure for severe disease (classes III and IV), age greater than 75 years (OR 2.3, 95% CI 1.2 to 4.4, $p = 0.011$), high CRP (OR 4.4, 95% CI 2.4 to 7.6, $p < 0.0001$), high LDH (OR 2.7, 95% CI 1.4 to 5.0, $p = 0.027$), AEP (OR 3.2, 95% CI 1.8 to 5.6, $p = 0.0001$), high NLR (OR 2.5, 95% CI 1.3 to 4.9, $p = 0.006$), and the presence of pulmonary comorbidities (OR 2.3, 95% CI 1.1 to 4.6, $p = 0.013$) emerged as independent predictors. COVID-19-associated death was independently predicted by age greater than 75 years (OR 8.3, 95% CI 3.5 to 19.8, $p < 0.0001$), high LDH (OR 4.2, 95% CI 1.8 to 10, $p = 0.0012$), high NLR (OR 2.8, 95% CI 2.1.1 to 7.4, $p = 0.035$), and AEP (OR 2.6, 95% CI 1.2 to 5.7, $p = 0.017$).

4. Discussion

Among other findings, COVID-19 is characterized by the infiltration of infected tissues by macrophages/monocytes, as well as lymphopenia and neutrophilia in the peripheral blood of patients. Innate immune cells are activated by viral components, resulting in enhanced interferon production. Moreover, the release of endothelial cytokines that increase capillary permeability leads to the activation of platelets, enhanced coagulation, reduced fibrinolysis, and overactivation of the complement system [1,3,16]. Together, these known pathomechanisms provide the rationale to include lymphocyte, neutrophil, monocyte, and platelet counts to assess complete-blood-count-based biomarkers to predict COVID-19 outcome [17]. The NLR, determined at the time of admission to the hospital, has been frequently used as a prognostic biomarker and was included in the present study as a comparator to more complex markers such as the PIV, which has not yet been studied in COVID-19 patients [17–19]. Indeed, our data confirm results of previous studies showing that the baseline NLR is an independent predictor of COVID-19-associated death and severity, as classified by the WHO. In comparison to the NLR, the SII, including not only neutrophils and lymphocytes, but also platelets, was more infrequently studied in COVID-19 patients [17]. Ballaz and Fors recently suggested that a complex interaction between inflammation and haemostasis may be the reason for the modest performance of SII in the prediction of severe COVID-19 [18]. Nonetheless, SII may serve as an indicator of the inflammation levels resulting from COVID-19, which could ultimately predict death [18]. In the present study, an SII greater than 1196 was significantly associated with COVID-19-associated death but failed to independently predict this outcome as assessed by multivariate analysis. In this regard, the NLR appears to outperform SII with respect to assessing COVID-19 mortality. In line with our findings, Karimi et al. showed, in their review on novel prognostic inflammatory biomarkers for COVID-19, that most previously studied parameters are able to predict COVID-19 prognosis; however, the NLR appears to be the most robust biomarker [17,18]. Since macrophages/monocytes are also involved in the progression to severe disease, we also included the PIV in our analysis, which incorpo-

rates monocyte counts [16]. However, the PIV did not turn out to be a significant predictor of COVID-19 outcome for any of the measures used in our study. Interestingly, it appears that PIV may be a more suitable biomarker for cancer patients [14,15].

The role of biomarkers, including age, CRP, ferritin, LDH, and comorbidities, have been extensively discussed in previous studies [1–3]. We have shown that the aforementioned parameters are more or less strong independent predictors for three outcome measures: COVID-19-associated death, disease severity according to clinical-therapeutic staging, as proposed by Siddiqi and Mehra staging, and the WHO clinical progression scale [12,13]. In our study population, almost 45% of patients presented with AEP on admission, and 74.5% patients had some degree of eosinopenia. Indeed, Soni reported that eosinopenia ($<50/\mu\text{L}$) on admission is a reliable and convenient early diagnostic biomarker for COVID-19 infection (sensitivity 80.7%, specificity 100%), aiding in the early identification, triaging, and isolation of patients until qPCR results are available [10]. However, eosinopenia was not significant as a prognostic predictor in that study [10]. Hence, we aimed to investigate a more stringent scenario using AEP as a dichotomous variable. In the literature, we found only two studies investigating AEP in the setting of COVID-19 [9,11]. Cazzaniga et al. studied 107 patients with COVID-19-associated pneumonia and observed that AEP was associated with clinical outcomes such as mortality [9]. Ito et al. observed that AEP was a significant risk factor for ICU admission in an Asian population ($n = 125$) [11]. However, they did not detect a significant correlation with 30-day mortality [11]. By investigating a larger cohort of patients, we have shown that AEP is an easily obtained and inexpensive hematologic biomarker with good prognostic accuracy for severe and fatal COVID-19. Indeed, eosinophils reportedly have an antiviral effect, including the rapid capture and inactivation of viruses and viral blood load [11,20].

Inherent to the study design, our mixed retrospective/prospective analysis was limited by data collected in a real-world clinical environment, potentially leading to information bias. Clinical judgments by treating clinicians directed data collection, possibly resulting in missing data and incomplete analyses. Given the overwhelming workload and pressure stressing the healthcare system during the first COVID-19 infection waves, some parameters of the hospital stay were not collected, leading, in some cases, to a lack of detail. Thus, we analysed all biomarkers only at the time of hospital admission and not longitudinally. Moreover, we mainly included patients hospitalized during the first infection waves in Germany, and as such our results cannot necessarily be extrapolated to other patient populations analysed during later waves. Finally, co-infection with other pathogens and comorbidities may also be confounding factors for this study with respect to COVID-19 death rates. However, the strengths of the present study include a reasonable sample size and the fact that AEP was correlated with three different outcome measures.

In conclusion, a further assessment of biomarkers that predict severe COVID-19 remains not only of vital importance with respect to mortality, but also for increased risk for the development of long COVID-19 [21,22]. As a prognostic marker for the disease severity of COVID-19, the NLR is superior to more complex biomarkers such as SII and PIV. More importantly, a decreased eosinophil count appears to be a hallmark of COVID-19 infection, with AEP emerging as a potential independent predictor for COVID-19 severity and mortality. Hence, further studies are needed, notably on larger, prospective cohorts, and probably as part of a multi-centre and multi-marker approach in order to further evaluate the prognostic power of easily available and inexpensive CBC-based parameters such as AEP in patients with COVID-19.

Author Contributions: T.G. conceived, designed, and planned the study. N.S. screened the patients, extracted the data, and performed some data analyses. T.G. performed the statistics. T.G., L.S., C.H.S., C.T.-R., J.C.B., O.O., A.R.-S. and W.S. were involved in data curation, supervision, project administration, and supervision. T.G. and N.S. drafted the manuscript and interpreted the data. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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