ORIGINAL ARTICLE

Prevalence and clinical outcomes of eosinophilia in critically ill patients

Mona-Rita Yacoub[1,2,†], Maria Bernadette Cilona[1,†], Levan Berikashvili[3], Mikhail Yadgarov[3], Petr Polyakov[3], Giovanni Landoni[1,2], Artem Kuzovlev[3], Alexey Yakovlev[3], Kristina Kadantseva[3], Elizaveta Korolenok[3], Valery Likhvantsev[3,4]

[1]IRCCS San Raffaele Scientific Institute, Milan, Italy

[2]School of Medicine, Vita-Salute San Raffaele University, Milan, Italy

[3]Federal Research and Clinical Centre of Intensive Care Medicine and Rehabilitology, Moscow, Russia

[4]I. Sechenov First Moscow State Medical University, Moscow, Russia

[†]These authors contributed equally to this work

Summary

Background. Eosinophilia in hospitalized patients is associated with increased mortality. However, eosinophilia was poorly investigated in the intensive care unit (ICU). The aim of our study was to investigate the prevalence of eosinophilia and its association with clinical outcomes in critically ill patients. **Methods.** This retrospective cohort study analyzed data from the Russian Intensive Care Dataset. The primary endpoint was the prevalence of eosinophilia (>0.5 × 10^9/L) in ICU patients. The secondary endpoints included all-cause hospital mortality, mechanical ventilation and vasoactive drug use. Subgroup analysis was performed for patients with mild eosinophilia (0.5-1.5 × 10^9/L) and hypereosinophilia (>1.5 × 10^9/L). **Results.** Among the 2,082 patients included in the analysis, 406 (19%) developed eosinophilia during ICU stay, including 362 (17%) with mild eosinophilia and 44 (2%) with hypereosinophilia. Out of 2,082 patients,

1,676 (81%) did not develop eosinophilia, and 406 (19%) developed eosinophilia during ICU stay. Compared with patients without eosinophilia, patients in the eosinophilia group had longer hospital stay (41 [24-63] *versus* 32 [22-48] $p < 0.001$) and more frequently required mechanical ventilation (236 [58.1%] *versus* 722 [43.1%], $p < 0.001$) and vasoactive drugs (83 [24.6%] versus 226 [17.0%], $p < 0.001$). Mortality was higher in hypereosinophilia group compared with patients without eosinophilia (13 [29.5%] *versus* 201 [12%], $p < 0.001$). **Conclusions.** Patients with eosinophilia had longer hospital stays, increased requirement of mechanical ventilation and vasopressor support compared with patients without eosinophilia. Eosinophilia could represent a disease severity marker.

Key words

Eosinophilia; hypereosinophilia; organ damage; intensive care unit; critically ill.

IMPACT STATEMENT

Eosinophilia in critically ill patients is common and associated with longer hospitalization, higher need for organ support, and increased mortality, suggesting its potential role as a marker of disease severity.

Introduction

Eosinophilia is a common condition characterized by elevated eosinophil levels with potential clinical implications. It is defined as an eosinophil count over 500 cells/mm³, with hypereosinophilia being 1500 cells/mm³ or higher (1). Under physiological conditions, eosinophils represent only a small percentage of both circulating and tissue-resident white blood cells (2). Increased peripheral eosinophils play a significant role in promoting inflammation and organ damage (3). Eosinophils can rapidly release cytotoxic and procoagulant mediators and secrete proinflammatory interleukins (3, 4). Additionally, eosinophils release inflammatory mediators generating and maintaining an immunoinflammatory response also at tissue level perpetuating organ damage (5, 6).

Common causes of eosinophilia include atopic and allergic diseases, parasitic and viral infections, mycobacterial infections, hematologic disorders, and potentially fatal systemic adverse drug reactions (7). The occurrence of eosinophilia is not rare in hospitalized patients, and it seems to contribute to reduced survival and worse clinical outcomes (8-12). Additionally, when associated with specific signs and symptoms, eosinophilia can readily represent an important diagnostic indicator (1).

Despite growing evidence on the role of increased eosinophil counts in the inflammatory response and organ damage (13), eosinophilia has been poorly investigated in the intensive care unit (ICU) (14, 15). In the ICU, where there is a high prevalence of severe and life-threatening conditions (16), the occurrence of eosinophilia and hypereosinophilia necessitates careful evaluation to understand its prevalence and clinical implications.

For these reasons, we performed a retrospective analysis of patients admitted to the ICU to assess the prevalence of eosinophilia. The aim of our study was to investigate the prevalence of eosinophilia and its association with clinical outcomes.

Methods

This retrospective, single-center cohort study utilized the Russian Intensive Care Dataset (RICD) developed by the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology (17). This dataset includes clinical data from 7,730 hospitalizations of 5,115 patients, covering data from 3,291 hospitalizations in intensive care units (ICUs). The data encompassed all patients admitted between December 2017 and July 2023. All patient data were fully anonymized, and the local ethical committee approved the study without requiring for consent.

Patients

All adult patients admitted to the ICUs, for whom blood eosinophil counts were determined during primary hospitalization, were included in the study. The exclusion criteria were as follows: (1) non-primary ICU admission at a medical center, (2) an ICU stay of less than 24 hours, and (3) patients with missing information on ICD-10 diagnoses. Eosinophilia was defined as the highest value of an absolute eosinophil blood count>0.5 ×10^9/L during the ICU stay.

Data extraction

The data were extracted using SQLite version 3.45.2 (https://www.sqlite.org/). We extracted demographic, anthropometric, clinical and laboratory data. History of allergy was defined as a documented diagnosis of allergic disease reported in the patient's medical record, including respiratory allergic diseases (such as allergic rhinitis or asthma), drug hypersensitivity reactions, or other clinically documented allergic conditions. We also extracted data on hospital mortality, length of hospital stay, need for mechanical ventilation, use of vasoactive drugs, and discharge location.

Outcomes

The primary endpoint was the prevalence of eosinophilia in ICU patients. The secondary endpoints were all-cause hospital mortality, mechanical ventilation and vasoactive drug use, and duration of hospitalization. We compared patients with favorable and unfavorable outcomes. Unfavorable outcome was defined as the occurrence of in-hospital death or transfer from the hospital general ward to the ICU due to clinical worsening and need for intensive care support.

Statistical analysis

Data distribution was assessed via the Lilliefors test. Continuous variables are reported as medians (Me) and interquartile ranges (IQRs) and means with standard deviations (SDs), whereas categorical variables are expressed as frequencies and percentages. The chi-square test and Fisher's exact test were used to compare

categorical variables. Bonferroni correction was used if applicable. The Kruskal–Wallis test with Dunn–Bonferroni post hoc analysis and the Mann–Whitney U test (Wilcoxon rank-sum test) were applied for continuous variables.

Survival analysis was performed via Kaplan–Meier survival curves, and differences in survival between groups were evaluated using the log-rank test.

The strength of the associations between the parameters was evaluated via Spearman's rank correlation coefficient. Missing data were not imputed. Statistical significance was set at $p < 0.05$ (two-sided). All the statistical calculations were performed using IBM SPSS Statistics v. 27.0 and Stata v. 18.0.

Patients were classified into specific groups based on the maximum blood eosinophil levels observed during hospitalization. Mild eosinophilia was defined as a blood eosinophil count of 0.5-1.5 × 10^9/L at least once during hospitalization, and hypereosinophilia was defined as a blood eosinophil count >1.5 × 10^9/L.

Subgroup analysis was performed for patients with mild eosinophilia and hypereosinophilia.

Results

Baseline characteristics

Among the 2,479 patients admitted to the ICU within the study period, 2,082 patients fulfilling the study criteria were included. Among the 2,082 patients, 1676 (81%) did not develop eosinophilia, and 406 (19%) developed eosinophilia during the ICU stay. Out of 406 patients who developed eosinophilia, 362 (17%) had mild eosinophilia, and 44 (2%) had hypereosinophilia (Figure 1). The baseline characteristics of the study population are summarized in Table I.

Patients who developed eosinophilia had higher eosinophil count at baseline (0.3 [0.1-0.5] versus 0.1 [0.0-0.2], $p<0.001$) compared with patients without eosinophilia. In addition, patients with eosinophilia were younger (60 [45-71] versus 62 [49-73] years, $p=0.01$), had higher SOFA score (3 [2-5] versus 3 [1-4],

p<0.001), lower GCS score (11 [8-14] versus 13 [10-15], p<0.001), and higher levels of troponin, C-reactive protein, and white blood cells at baseline compared with patients without eosinophilia. Additionally, polytrauma was more prevalent among patients who developed eosinophilia compared with patients without eosinophilia (23 [5.7%] versus 48 [2.9%], p<0.005). Baseline characteristics of patients with and without eosinophilia are reported in Table I. Correlations between eosinophilic count and baseline characteristic show only very weak correlation (Supplemental table II, supplemental figure 1-4).

Patients with mild eosinophilia and hypereosinophilia had a higher eosinophil counts at baseline compared with patients without eosinophilia, respectively 0.3 [0.1-0.5] versus 0.1 [0.0-0.2] (p<0.01) and 0.2 [0.0-0.7] versus 0.1 [0.0-0.2] (p<0.01). Polytrauma was more frequent in mild eosinophilia group (48 [2.9%] versus 21 [5.8%], p=0.02) and in the hypereosinophilia group (48 [2.9%] versus 2 [4.5%], p<0.001), compared with patients without eosinophilia. In addition, mental and cognitive disorders were more frequently reported in patients with mild eosinophilia compared with patients without eosinophilia (96 [26.5%] versus 354 [21.1%], p< 0.001) and with patients with hypereosinophilia (96 [26.5%] versus 6 [13.6%], p< 0.001). Upon admission, the SOFA score was higher in the mild eosinophilia group (3 [2-5] versus 3 [1-4], p<0.001) and in hypereosinophilia group (4 [3-6] versus 3 [1-4], p=0.002) compared with patients without eosinophilia. The comparison between patients without eosinophilia, mild eosinophilia, and hypereosinophilia is reported in Supplementary Table I.

Outcomes

Patients in the eosinophilia group had an higher length of hospital stay (41 [24-63] days versus 32 [22-48] days p<0.001), more frequently required mechanical ventilation (236 [58.1%] versus 722 [43.1%], p<0.001), and vasoactive drugs (83 [24.6%] versus 226 [17.0%], p<0.001) compared with patients without eosinophilia. In addition, they were more frequently transferred to other ICU (206 [50.7%] versus 582 [34.7%], p<0.001) and had more frequently unfavorable outcome (249 [61.3] versus 783 [46.7%], p<0.001) (Table II).

Mortality was higher in hypereosinophilia group compared with patients without eosinophilia (13 [29.5%] versus 201 [12%], p<0.001) and with mild eosinophilia group (13 [29.5%] versus 30 [8.3%], p<0.001). In addition, hypereosinophilia group had more frequently unfavourable outcome compared with patients without eosinophilia (34 [77.3%] versus 783 [46.7%], p<0.001) and with mild eosinophilia group (34 [77.3%] versus 215 [59.4%], p<0.001), and were less frequently discharged (10 [22.7%] versus 893 [53.3%], p<0.001) and (10 [22.7%] versus 147 [40.6%], p<0.001). Moreover, hypereosinophilia group compared with patients without eosinophilia had longer of hospital stay (48.5 [23.5-68.5] days vs 32 [22-48] days, p=0.02), more frequently required mechanical ventilation (28 [63.6%] versus 722 [43.1%], p=0.02), and use of vasoactive drugs (13 [33.3%] versus 226 [17%], p=0.02). Similar finding was observed when comparing mild eosinophilia with patients without eosinophilia (Supplemental Table III).

The Kaplan-Meier analysis comparing patients without eosinophilia with patients with eosinophilia group (including both mild eosinophilia and hypereosinophilia) further showed a higher mortality risk over time in the eosinophilia group (Figure 2). Similarly, the Kaplan-Meier survival curves demonstrated a statistically significant increased risk of mortality over time in patients with mild eosinophilia and hypereosinophilia compared to patients without eosinophilia (Supplemental figure 5). This trend was stronger in the hypereosinophilia group compared with both mild eosinophilia group and patients without eosinophilia.

Characteristics of the favorable and unfavorable outcome groups

The prevalence of patients without eosinophilia was higher in the favorable outcome group (85%) compared to the unfavorable outcome group (75.9%). Eosinophilia was present in 15% of individuals with favorable outcomes and 24% with unfavorable outcomes (Table III). We found eosinophilia in 17.6% of deceased patients, 26.1% of ICU transferred patients, and 15% of those not charged (Supplemental table IV).

Mild eosinophilia was more prevalent in the unfavorable outcome group (20.8%) than in the favorable group (14%). Hyper-eosinophilia was rare but higher in the unfavorable outcome group (3.3%) compared to only 1% in the favorable group.

Mild eosinophilia was more common in the transferred group (23.5%) compared to the dead (12.3%) and discharged groups (14%). Hypereosinophilia was higher in the dead group (5.3%) than in ICU transfered (2.7%) and in discharged group (1%).

Discussion

In our retrospective analysis, we found that the prevalence of mild eosinophilia was 17% and of hypereosinophilia was 2% in our cohort of ICU patients. Additionally, patients with eosinophilia had a longer length of hospital stay and were more likely to require mechanical ventilation and vasopressor support, compared with patients without eosinophilia. These findings were more pronounced in the hypereosinophilia group, where we observed an increased mortality compared with patients without eosinophilia or with mild eosinophilia. Our findings suggest that eosinophilia could be a potential marker of disease severity in critically ill patients.

This is the first study comparing patients with eosinophilia versus those with normal eosinophil counts in the ICU. Gaillet et al., in their retrospective analysis of 66,040 ICU admissions, found that the incidence of eosinophilia was 0.9%, with an ICU mortality of 18.4% in patients who developed eosinophilia after ICU admission (14). However, they did not compare patients with eosinophilia to those with normal blood eosinophil counts. The discrepancy in the prevalence of eosinophilia reported by Gaillet et al. compared with our analysis can be attributed to the exclusion of patients with an eosinophil count between 500 and 1000 cells/microliter from the eosinophilia group". Previous studies conducted in other settings suggest that eosinophilia correlates with disease severity. For example, Chen et al., in their retrospective analysis of 7,835 patients with eosinophilia found that patients with moderate to severe eosinophilia were more likely admitted to ICU (15). Similarly, Rao et al., observed that increased eosinophil counts were correlated with hospital mortality in patients with acute heart failure

and dilated cardiomyopathy. (18). In contrast, Merino et al., in their prospective observational study of septic patients, reported that eosinophil counts were lower in those who died of sepsis than in those who survived (19). Additionally, previous studies reported that eosinophil counts negatively correlate with adverse events in COVID-19 patients (20, 21). These findings are inconsistent with our results, likely because septic patients comprised only 0.5% of our cohort, and there were no COVID-19 patients. Indeed, persistent peripheral eosinopenia has been identified as a marker of the severity of bacterial sepsis and is independently associated with poor outcomes (22). In the context of acute respiratory distress syndrome, eosinophil counts in bronchoalveolar lavage are initially low during the early phase of disease but increase in the later stages. (22, 23).

Our findings could represent a significant advancement in the management of ICU patients, allowing for more accurate risk stratification and facilitating the adoption of personalized therapeutic approaches. A rapid, simple, and low-cost peripheral blood eosinophil count test can be used as a marker of severity in critically ill patients. The ability to identify high-risk patients early could enable more efficient allocation of medical resources and improve clinical outcomes. This includes planning for potential increased needs for respiratory support, specialized diagnostic tests, and targeted therapies.

We observed increased requirements for mechanical ventilation and ventilatory support among patients with eosinophilia. This finding highlights the importance of closely monitoring this population, as they may require timely and intensive interventions to prevent clinical worsening. We also found high hospital mortality in patients with hypereosinophilia. These findings emphasize the need for accurate differential diagnosis for patients with hypereosinophilia, as these patients may represent a high-risk population for worse clinical outcomes. Indeed, recent guidelines have proposed algorithms that provide recommendations for the clinical follow-up and management of patients with hypereosinophilia (24).

Finally, longer hospital stays in patients with eosinophilia imply increased healthcare costs. These data can have significant implications for healthcare policy, suggesting the need for policies that focus on this population.

To the best of our knowledge, this is the first study comparing patients with eosinophilia with patients with normal blood eosinophil counts in the ICU. Another strength is that it includes a heterogeneous population of patients from the ICU, increasing the generalizability of the results. In addition, the study design included three different groups, allowing for direct comparisons between patients with normal blood eosinophil counts and mild and hypereosinophilia.

However, it is important to acknowledge certain limitations associated with this study. First, as an observational study, causality between eosinophilia and clinical outcomes. Second, the retrospective design of the study may lead to biases related to data collection, as it relies on previously recorded information. Additionally, the relatively small sample size limits the statistical power of the study and may affect the generalizability of the findings. Indeed, the small number of patients with hypereosinophilia reduces the statistical power for subgroup analyses. Therefore, our findings should be considered interpreted cautiously and larger prospective multicenter studies are needed to confirm the potential role of eosinophilia in critically ill patients. Finally, we did not collect data on the progression of eosinophilia over time; therefore, we cannot determine whether variations in eosinophilia correlate with outcomes. Indeed, in our cohort, most patients developed eosinophilia during hospitalization rather than at ICU admission. Future studies are needed to investigate whether early versus delayed eosinophilia may have different prognostic implications.

Another limitation of the present study is that the underlying cause of eosinophilia was not systematically investigated. In particular, detailed information regarding drug exposure and its temporal relationship with the onset of eosinophilia was not consistently available, preventing a reliable identification of drug-induced eosinophilia in this cohort. Due to the retrospective design and the large heterogeneity of critically ill patients included in this cohort, it was not possible to reliably determine the specific etiology of eosinophilia in each case. Eosinophilia in ICU patients may arise from multiple conditions. Therefore, the present analysis focused on the association between eosinophilia and clinical outcomes rather than on the etiological characterization of eosinophilia. Future prospective studies should specifically investigate the causes and clinical significance of eosinophilia in critically ill patients.

Conclusions

Eosinophilia was associated with a long length of hospital stay, as well as increased requirements for mechanical ventilation and vasopressor support. Hypereosinophilia, in particular, was linked to increased hospital mortality. These findings suggest that eosinophilia could serve as a marker of disease severity in critically ill patients. Further prospective studies with large sample size would provide better understanding of the role of eosinophilia in critically ill patients.

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Conflict of interests

The authors declare no conflicts of interests.

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Table I. Baseline characteristics of patients without eosinophilia and with eosinophilia (eosinophil count > 500 cells/microlitre).

	Without eosinophilia (N=1676)	**Eosinophilia (N=406)**	**p-value**
Sex (male)	931 (55.5 %)	230 (56.7 %)	n.s.
Age	62 (49-73)	60 (45-71)	0.012
White blood cells	8.3 (6.5-11)	9.8 (7.7-12.7)	<0.001
Neutrophils (×10³/μL)	6.0(4.2-8.6)	7.2 (5.1-9.5)	<0.001
Eosinophils (×10³/μL)	0.1 (0.0-0.2)	0.3 (0.1-0.5)	<0.001
Eosinophils (%)	1.2 (0.5-2.2)	2.6 (1.1-5.2)	<0.001
C-reactive protein	37 (13-83)	47 (25-100)	<0.001
Troponin	0.1 (0.0-27.1)	0.0 (0.0-0.1)	0.04
Hypocoagulable state	7 (0.4 %)	1 (0.2 %)	n.s.
Polyneuropathy	11 (0.7 %)	3 (0.7 %)	n.s.
Heart failure	348 (20.8 %)	69 (17 %)	n.s.
Acute myocardial infarction	6 (0.4 %)	3 (0.7 %)	n.s.

Sepsis	9 (0.5 %)	2 (0.5 %)	n.s.
Polytrauma	48 (2.9 %)	23 (5.7 %)	0.005
Malignant tumor	49 (2.9 %)	8 (2 %)	n.s.
Hypertension	1052 (62.8 %)	249 (61.3 %)	n.s.
Allergy	4 (0.2 %)	3 (0.7 %)	n.s.
GCS	13 (10-15)	11 (8-14)	<0.001
SOFA	3 (1-4)	3 (2-5)	<0.001

Abbreviations: n.s., non significant; GCS, Glasgow coma scale; SOFA, sequential organ failure assessment

Table II. Outcome in patients without eosinophilia versus patients with eosinophilia.

Outcome	**Without eosinophilia (N=1676)**	**Eosinophilia (N=406)**	**p-value**
Hospital Mortality	201 (12 %)	43 (10.6 %)	n.s.
Median hospital length of stay [IQR], days	32 [22-48]	41 [24-63]	<0.001
Mechanical ventilation	722 (43.1 %)	236 (58.1 %)	<0.001
Use of vasoactive drugs	226 (17.0 %)	83 (24.6 %)	<0.001
Patients transferred to other ICU	582 (34.7 %)	206 (50.7 %)	<0.001
Patients discharged	893 (53.3 %)	157 (38.7 %)	<0.001
Patients with favorable outcome	893 (53.3 %)	157 (38.7 %)	<0.001
Patients with unfavorable outcome	783 (46.7 %)	249 (61.3 %)	<0.001

Abbreviations: n.s., non significant

Table III. Comparison between favorable versus unfavorable outcome groups.

Outcome	Favorable (N=1050)	Unfavorable (N=1032)	p-value
Sex (male)	609 (58 %)	552 (53.5 %)	0.04
Age	60 (45-70)	65 (51-75)	<0.001
Acute myocardial infarction	1 (0.1 %)	8 (0.8 %)	0.02
Pneumonia	240 (22.9 %)	484 (46.9 %)	<0.001
Sepsis	2 (0.2 %)	9 (0.9 %)	0.03
Hypocoagulable state	4 (0.4 %)	4 (0.4 %)	n.s.
Malignant tumor	20 (1.9 %)	37 (3.6 %)	0.02
Diabetes (insulin independent)	36 (3.4 %)	74 (7.2 %)	<0.001
Mental and cognitive disorders	200 (19 %)	256 (24.8 %)	<0.001
Heart failure	213 (20.3 %)	204 (19.8 %)	n.s.
Valvular heart disease	4 (0.4 %)	13 (1.3 %)	0.03
Polytrauma	35 (3.3 %)	36 (3.5 %)	n.s.
Chronic ischemic heart disease	133 (12.7 %)	272 (26.4 %)	<0.001
Chronic obstructive pulmonary disease	4 (0.4 %)	11 (1.1 %)	n.s.
Atrial fibrillation	21 (2 %)	51 (4.9 %)	<0.001
Chronic kidney disease	8 (0.8 %)	23 (2.2 %)	0.006
Without eosinophilia	893 (85 %)	783 (75.9%)	<0.001
Eosinophilia	157 (15 %)	249 (24.1%)	<0.001
Mild eosinophilia	147 (14 %)	215 (20.8%)	<0.001
Hypereosinophilia	10 (1 %)	34 (3.3%)	<0.001

Abbreviations: n.s., non significant.

Figure 1. Flowchart of the included patients.

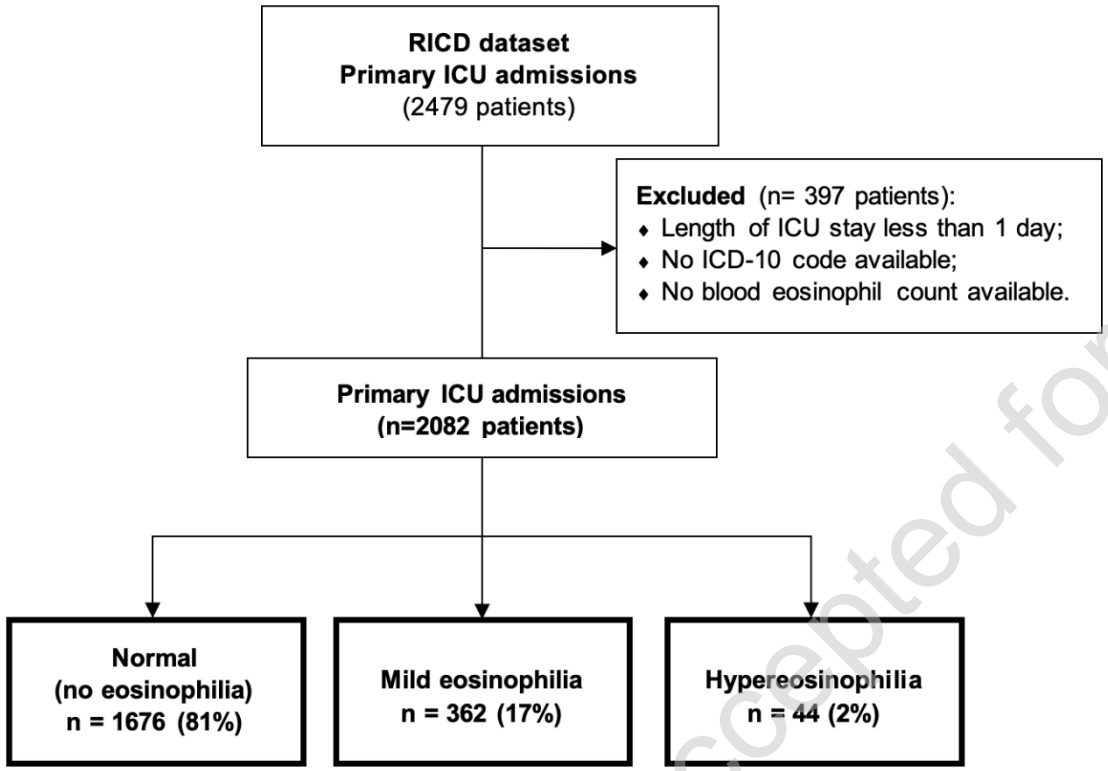
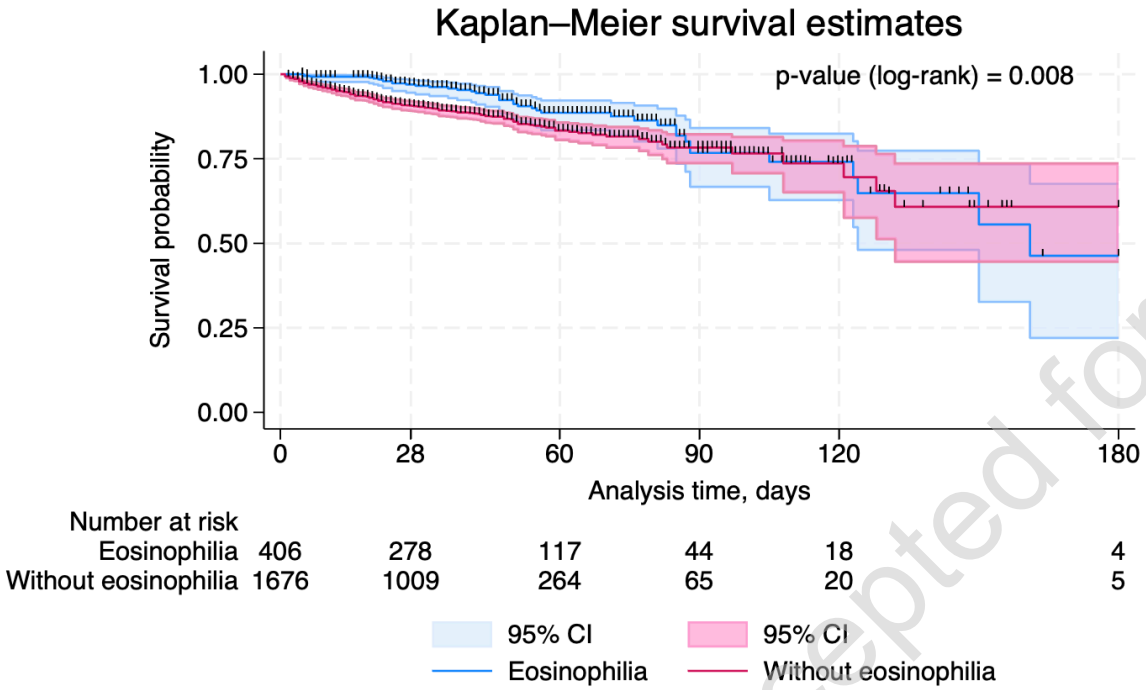


Figure 2. Kaplan-Meier of mortality between patients without eosinophilia, mild eosinophilia, and hypereosinophilia.



Supplementary material

Supplemental table I. Baseline Characteristics of the Normal (no eosinophilia), Mild eosinophilia (500-1500 cells/microlitre), and Hypereosinophilia (eosinophil count >1500) Groups at Admission.

	Without eosinophilia	Mild eosinophilia	Hypereosinophilia	1 vs 2 vs 3,	1 vs 2,	1 vs 3	2 vs 3

	(N=1676)	(N=362)	(N=44)	p-value	p-value	p-value	p-value
Sex (male)	931 (55.5 %)	203 (56.1 %)	27 (61.4 %)	n.s.	n.s.	n.s.	n.s.
Age	62 [49-73]	59.5 [47-71]	61.5 [41.5-71]	0.04	0.05	0.92	n.s.
White blood cells	8.3 [6.5-11]	9.7 [7.6-12.6]	10.2 [8.5-13.15]	<0.001	<0.001	0.003	n.s.
Eosinophils (absolute count)	0.1 [0.04-0.2]	0.3 [0.1-0.5]	0.2 [0.0-0.7]	<0.001	<0.001	<0.001	n.s.
Eosinophils (%)	1.2 [0.5-2.2]	2.6 [1.1-5.2]	2 [0.5-5.7]	<0.001	<0.001	0.008	n.s.
C-reactive protein	37 [13-83]	48 [26-101]	41 [22-72]	<0.001	<0.001	n.s.	n.s.
Hypocoagulable state	7 (0.4 %)	1 (0.3 %)	0 (0 %)	n.s.	n.s.	n.s.	n.s.
Polyneuropathy	11 (0.7 %)	3 (0.8 %)	0 (0 %)	n.s.	n.s.	n.s.	n.s.
Heart failure	348 (20.8 %)	59 (16.3 %)	10 (22.7 %)	n.s.	n.s.	n.s.	n.s.
Acute myocardial infarction	6 (0.4 %)	3 (0.8 %)	0 (0 %)	n.s.	n.s.	n.s.	n.s.
Sepsis	9 (0.5 %)	1 (0.3 %)	1 (2.3 %)	n.s.	n.s.	n.s.	n.s.
Polytrauma	48 (2.9 %)	21 (5.8 %)	2 (4.5 %)	0.03	<0.001	<0.001	<0.001
Malignant tumor	49 (2.9 %)	7 (1.9 %)	1 (2.3 %)	n.s.	n.s.	n.s.	n.s.
Mental and cognitive disorders	354 (21.1 %)	96 (26.5 %)	6 (13.6 %)	0.03	<0.001	<0.001	<0.001
Hypertension	1052 (62.8 %)	223 (61.6 %)	26 (59.1 %)	n.s.	n.s.	n.s.	n.s.
Allergy	4 (0.2 %)	3 (0.8 %)	0 (0 %)	n.s.	n.s.	n.s.	n.s.
GCS	13 [10-15]	11 [8-14]	11 [8-11.5]	<0.001	<0.001	<0.001	n.s.
SOFA	3 [1-4]	3 [2-5]	4 [3-6]	<0.001	<0.001	0.002	n.s.

Abbreviations: n.s., non significant; GCS, Glasgow coma scale; SOFA, sequential organ failure assessment

Supplemental table II. Correlation of eosinophil counts with laboratory parameters and clinical scales (blue shades indicate a negative correlation; red shades indicate a positive correlation).

	N	p-value	Spearman's correlation coefficient R
Procalcitonin	1316	<0.001	-0.27
Neutrophil-to-lymphocyte ratio	23220	<0.001	-0.25
APACHE II	122	0.007	-0.24
Lactate	2427	<0.001	-0.21
Troponin	549	<0.001	-0.20
SOFA	4462	<0.001	-0.20
C-reactive protein	19248	<0.001	-0.18
Neutrophils	23221	<0.001	-0.10
Lactate dehydrogenase	5097	<0.001	-0.06
Aspartate aminotransferase	20268	<0.001	-0.06
Alanine transaminase	20251	<0.001	-0.05
Amylase	12969	0.805	0.00
Creatinine	20946	0.008	0.02

White blood cells	23222	<0.001	0.03
FOUR	2193	<0.001	0.11
GCS	2292	<0.001	0.12
Total protein	20455	<0.001	0.16
Lymphocytes	23221	<0.001	0.29
Basophils	23081	<0.001	0.31

Supplemental table III. Outcome in patients with hypereosinophilia, mild eosinophilia and without eosinophilia

Outcome	**Normal (no eosinophilia) (N=1676)**	**Mild eosinophilia (N=362)**	**Hypereosinophilia (N=44)**	**1 vs 2 vs 3 p-value**	**1 vs 2 p-value**	**1 vs 3 p-value**	**2 vs 3 p-value**
Hospital Mortality	201 (12 %)	30 (8.3 %)	13 (29.5 %)	<0.001	n.s.	0.01	<0.001
Median hospital length of stay [IQR], days	32 [22; 48]	41 [24; 63]	48.5 [23.5; 68.5]	<0.001	<0.001	0.02	n.s.
Mechanical ventilation	722 (43.1 %)	208 (57.5 %)	28 (63.6 %)	<0.001	<0.001	0.02	n.s.
Use of vasoactive drugs	226 (17 %)	70 (23.4 %)	13 (33.3 %)	0.002	0.03	0.02	n.s.
ICU Transfer	582 (34.7 %)	185 (51.1 %)	21 (47.7 %)	<0.001	<0.001	<0.001	<0.001
Discharged	893 (53.3 %)	147 (40.6 %)	10 (22.7 %)	<0.001	<0.001	<0.001	<0.001
Favorable	893 (53.3 %)	147 (40.6 %)	10 (22.7 %)	<0.001	<0.001	<0.001	0.063

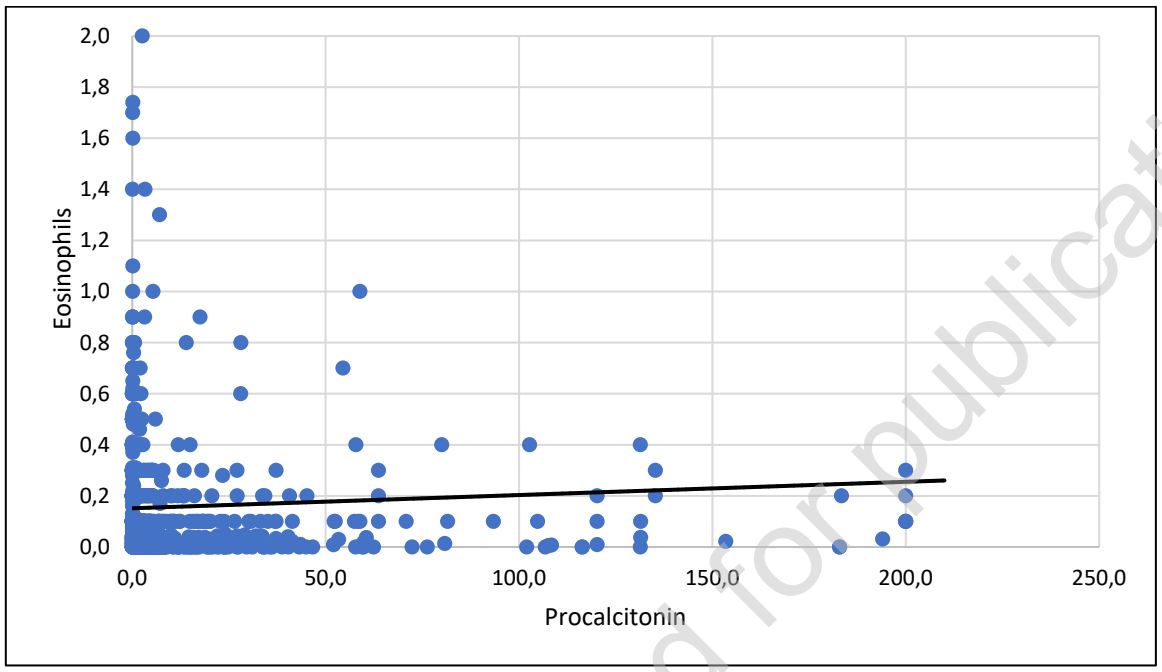
Unfavorable	783 (46.7 %)	215 (59.4 %)	34 (77.3 %)	<0.001	<0.001	<0.001	0.063

Abbreviation: ICU, intensive care unit

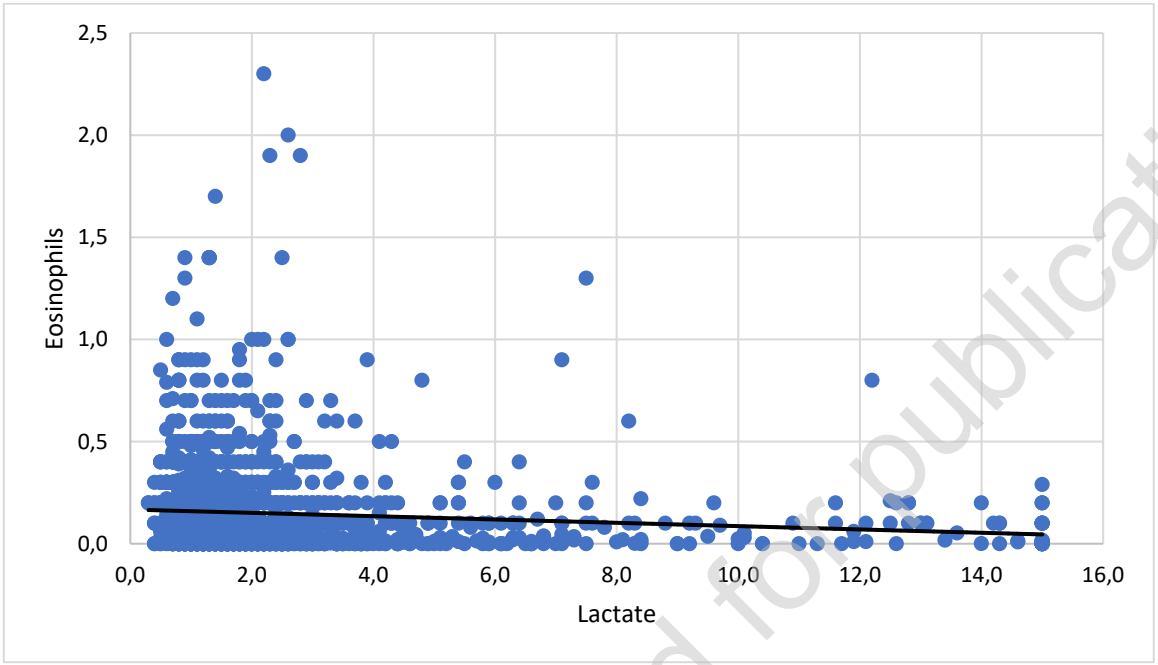
Supplemental table IV. Comparison between dead, ICU transferred and discharged patients.

Outcomes	Dead (N=244)	ICU Transfer (N=788)	Discharged (N=1050)	1 vs 2 vs 3 p-value	1 vs 2 p-value	1 vs 3 p-value	2 vs 3 p-value
Without eosinophilia	201 (82.4 %)	582 (73.9 %)	893(85%)	<0.001	<0.001	<0.001	<0.001
Eosinophilia	43 (17.6 %)	206 (26.1 %)	157(15%)	<0.001	0.02	n.s.	<0.001
Mild eosinophilia	30 (12.3 %)	185 (23.5 %)	147(14%)	<0.001	<0.001	<0.001	<0.001
Hypereosinophilia	13 (5.3 %)	21 (2.7 %)	10(1%)	<0.001	n.s.	<0.001	0.01

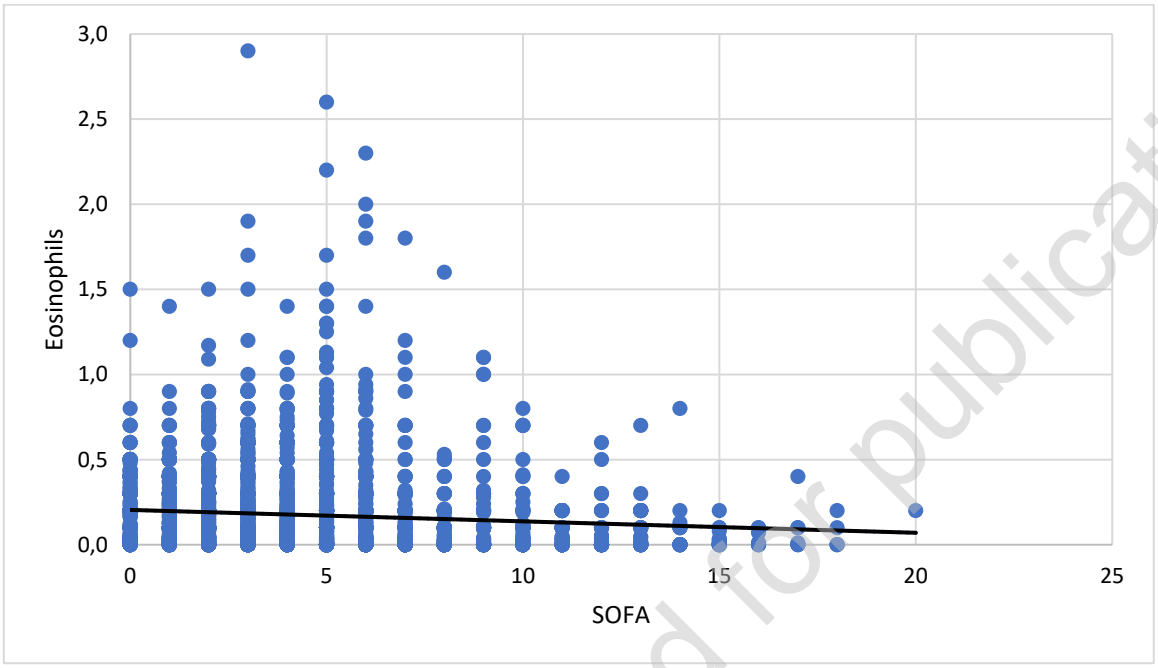
Supplemental figure 1. Scatter diagram for correlation between eosinophil counts and procalcitonin levels.



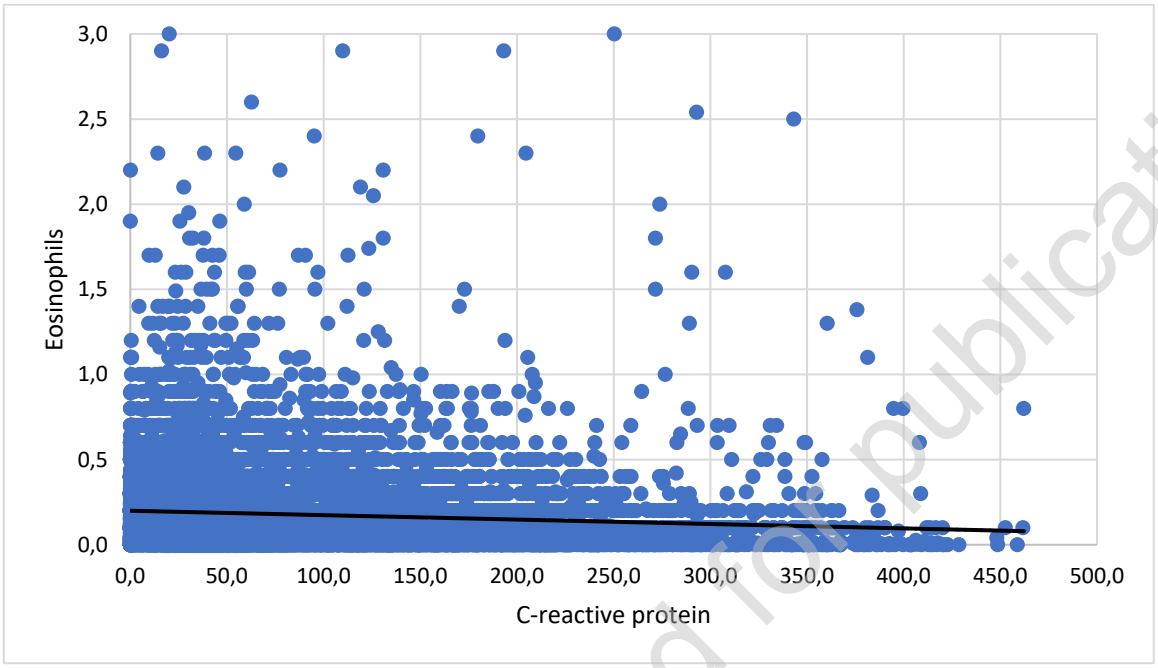
Supplemental figure 2. Scatter diagram for correlation between eosinophil counts and lactate levels.



Supplemental figure 3. Scatter diagram for correlation between eosinophil counts and Sequential Organ Failure Assessment (SOFA) Score.



Supplemental figure 4. Scatter diagram for correlation of eosinophil counts with C-reactive protein levels.



Supplemental figure 5. Kaplan-Meier of mortality in patients without eosinophilia, with mild eosinophilia, and with hypereosinophilia.