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Blood eosinopenia (≤30/µL) as an early predictor of respiratory failure in community-acquired pneumonia: A prospective multicentre study

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ABSTRACT

Introduction and objectives: Lower blood eosinophil counts have been associated with increased mechanical ventilation rates in patients with community-acquired pneumonia (CAP). However, the optimal eosinophil count threshold for identifying CAP patients at high risk of respiratory failure remains undefined. This study aimed to establish an optimal admission eosinophil count as a prognostic biomarker for respiratory failure in CAP.

Methods: This prospective, multicentre cohort study (PROGRESS) enrolled adult patients (≥18 years) hospitalised with community-acquired pneumonia (CAP). A receiver operating characteristic curve analysis with Youden's index was applied to identify the optimal eosinophil threshold for predicting mechanical ventilation. Associations were adjusted for corticosteroid use using multivariable regression. Additional outcomes – ICU admission and hospital length of stay – were compared between patients above and below the optimal eosinophil count threshold.

Results: An eosinophil count threshold of ≤30/µL was optimal for predicting mechanical ventilation. Patients with eosinophil counts ≤30/µL experienced significantly higher mechanical ventilation rates (15.5% versus 7.3%; $p < 0.0001$; RR 2.12, 95% CI 1.61–2.80), regardless of glucocorticoid treatment. They also exhibited higher ICU admission rates (23.1% versus 10.9%; $p < 0.0001$; RR 2.11, 95% CI 1.70–2.63) and longer hospital stays among survivors (median 8.0 versus 7.0 days; $p < 0.0001$).

Conclusions: Admission eosinopenia (≤30 µL) is a robust, easily measured biomarker that predicts respiratory failure in hospitalised CAP. It supports early risk stratification and may guide timely escalation of care.

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KEYWORDS
Pneumonia; blood eosinophil count; risk stratification; biomarker

Introduction

Lower respiratory tract infections, including community-acquired pneumonia (CAP), are major contributors to morbidity and mortality worldwide.[1] In-hospital mortality rates for CAP vary widely, ranging from 1.8% to 35.8%.[2] Many studies[3–5] demonstrated that delayed admission to intensive care units is associated with adverse outcomes in CAP patients. Notably, CAP patients who initially receive care on general wards but subsequently deteriorate, requiring mechanical ventilation or vasopressor support, face a remarkably high

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30-day mortality rate of 49%.[6] Only 16% of CAP patients who die in hospital have received mechanical ventilation.[2] This underscores the critical need for early identification of CAP patients at high risk of respiratory failure upon hospital admission.

Previous studies[7–10] suggest that lower blood eosinophil counts are associated with increased mechanical ventilation rates in CAP patients. However, the optimum eosinophil count threshold for risk stratification has not been determined yet. This study therefore aimed to evaluate eosinophil counts continuously at hospital admission to identify the optimal eosinophil count threshold for predicting mechanical ventilation requirements, and compare outcomes including the need for ventilatory support and intensive care unit (ICU) admission between eosinopenic and non-eosinopenic patients.

Material and methods

Study design and setting

This prospective multicentre cohort study was conducted within the PROGRESS (Pneumonia Research Network on Genetic Resistance and Susceptibility for the Evolution of Severe Sepsis) network [clinicaltrials.gov; identifier: NCT02782013] in medical centres across Germany.[11]

Participants

Patients (≥18-years) hospitalised with CAP confirmed by pulmonary infiltrates on chest X-ray were enrolled.[11] Patients were excluded if they had been hospitalised for any reason within 28 days prior to the index admission for CAP. Patients with known HIV infection or AIDS, or those who had received immunosuppressive therapies within the previous six months – including anti-tumour treatment, non-steroidal immunosuppressive agents, radiation therapy, or systemic corticosteroids at doses ≥20 mg/day for ≥14 days – were not eligible. Additional exclusion criteria included poststenotic pneumonia associated with bronchial carcinoma, prior organ or bone marrow transplantation, chronic respiratory support via tracheostomy, cystic fibrosis, active tuberculosis, acute lung injury or acute respiratory distress syndrome of extrapulmonary origin, massive aspiration, sepsis with an extrapulmonary focus, acute pulmonary embolism, end-stage heart failure (NYHA class IV), or advanced liver disease (Child-Pugh C). Patients who were pregnant, breastfeeding, previously participated in the PROGRESS study, or whose treatment was subject to limitation of therapy were also excluded.

Variables and data collection

Age, sex, blood parameters including C-reactive protein (CRP), leukocyte count, procalcitonin, haematocrit, eosinophil count analysed using flow cytometry technology (XN-Series, Sysmex, Kobe, Japan), the presence of systemic glucocorticoid therapy (prednisone, prednisolone, methylprednisolone, and hydrocortisone) during the study, pre-existing comorbidities, risk stratification scores for CAP including Confusion, Respiratory rate, Blood pressure, Age ≥65 years score (CRB-65), Confusion, Urea, Respiratory rate, Blood pressure, Age ≥65 years score (CURB-65), Pneumonia Severity Index (PSI), Infectious Diseases Society of America/American Thoracic Society minor criteria (IDSA/ATS minor criteria), and Sequential Organ Failure Assessment score (SOFA), in-hospital mortality, both non-invasive and invasive mechanical ventilation rates, and ICU admission rates were captured based on the documentation within the framework of the PROGRESS study.[11]

Statistical analysis

Receiver operating characteristic curve analysis determined the optimal eosinophil count threshold for predicting mechanical ventilation using Youden's index. Sensitivity, specificity, and positive and negative predictive values were calculated for this threshold with 95% confidence intervals (CIs), respectively. The association between the optimal eosinophil count threshold and risk of mechanical ventilation was analysed using a multivariable logistic regression model, adjusting for age, CRP, creatinine, haematocrit,

glucocorticoid treatment, and sex. The best model was selected by Akaike Information Criterion and evaluated for goodness-of-fit with the Hosmer-Lemeshow test. After excluding patients on systemic glucocorticoids, a second logistic regression assessed mechanical ventilation rates with the same covariates except glucocorticoid treatment.

Patients were classified into two groups based on the optimal eosinophil count threshold: those with eosinopenia (eosinophil count at or below the threshold) and those without eosinopenia (eosinophil count above the threshold). Laboratory parameters and length of hospital stay among survivors between these groups were compared using the Mann-Whitney U test, with *p*-values corrected via the Benjamini-Hochberg procedure. Comorbidity prevalence, glucocorticoid use, mechanical ventilation, and ICU admission rates between the eosinopenia and non-eosinopenia groups were analysed using Fisher's exact test, with *p*-values corrected by the Benjamini-Hochberg procedure.

Descriptive statistics were reported as medians, and 25th and 75th percentiles. Percentages were used to report categorical variables distributions. *P*-values less than 0.05 were considered statistically significant. All computations and visualisations were carried out with Python (3.12) and the following packages: statsmodels (0.14.2), pandas (2.2.2), seaborn (0.13.2), numpy (1.26.4), scipy (1.14.0), matplotlib (3.9.2), scikit-learn (1.5.1) and PySpiro (0.1.0).

Results

Characteristics of the entire patient cohort

A total of 1,763 patients (median age 63 years; 60.0% male; median BMI 26.04 kg/m^2) were included in the analysis. Of these, 16.1% ($n = 284$) required admission to the intensive care unit (ICU) and 10.78% ($n = 190$) required mechanical ventilation. In-hospital mortality rate was 1.99% ($n = 35$). Baseline characteristics for the entire cohort are summarised in Table 1.

Threshold determination for eosinopenia as a prognostic biomarker for mechanical ventilation in CAP and its independent association in multivariable analyses

Receiver operating characteristic curve analysis identified an admission eosinophil count threshold of ≤30/µL as optimal for predicting an increased risk of mechanical ventilation, with an area under the curve of 0.63 (see Supplementary Figure S1). In a multivariable regression analysis ($n = 1,610$), an eosinophil count ≤30/µL was

Table 1. Characteristics of the entire patient cohort.

Variable Sample size n (%)	Overall group ($n = 1,763$)
Median age in years (25th–75th percentile) 1,763 (100.0)	63.0 (46.00–74.00)
Male sex, n (%) 1,763 (100.0)	1,058 (60.0)
Weight in kg, median (25th–75th percentile) 1,762 (99.9)	78.00 (66.00–90.00)
Body mass index in kg/m^2, median (25th–75th percentile) 1,760 (99.8)	26.04 (22.94–29.82)
Country of birth, n (%) 1,763 (100.0)	Germany: 1,452 (82.4) Poland: 55 (3.1) Turkey: 32 (1.8) Austria: 22 (1.2) Russia: 22 (1.2) Unknown: 40 (2.3) Remaining countries*: 140 (7.9)
Mechanical ventilation rate, n (%) 1,763 (100.0)	$n = 190$ (10.8%)
Intensive care admission rate, n (%) 1,763 (100.0)	$n = 284$ (16.1%)
Mortality, n (%) 1,763 (100.0)	35 (2.0%)

IDSA/ATS, Infectious Disease Society of America/American Thoracic Society; PSI, Pneumonia Severity Index; SOFA, Sequential Organ Failure Assessment.
*Remaining countries accounted for <1% of study participants, respectively.

independently associated with an increased risk of requiring mechanical ventilation ($p = 0.0001$), irrespective of glucocorticoid therapy. In a subsequent multivariable analysis restricted to patients not receiving glucocorticoids ($n = 1,232$), the association between eosinopenia (≤30/µL) and higher mechanical ventilation rates remained significant ($p = 0.0004$).

For the admission eosinophil count threshold of ≤30/µL, sensitivity, specificity, positive predictive value, and negative predictive value for predicting mechanical ventilation were 61.1% (95% CI 53.2–68.6%), 59.8% (95% CI 57.3–62.2%), 15.5% (95% CI 13.0–18.2%), and 92.7% (95% CI 91.5–93.8%), respectively.

Baseline characteristics by eosinophil count (≤30/µL versus >30/µL)

Of the 1,763 patients included in the analysis, 749 (42.5%) presented with eosinopenia (≤30/µL), and 1,014 (57.5%) had eosinophil counts >30/µL. Median eosinophil count was 0/µL (25th–75th percentile: 0–12/µL) versus 140/µL (25th–75th percentile: 80–250/µL) in the eosinopenia versus non-eosinopenia groups. Baseline demographic and clinical characteristics stratified by eosinophil group are summarised in Table 2.

Patients with eosinopenia had significantly higher levels of inflammatory markers, including CRP, procalcitonin, and total leukocyte count (all $p < 0.0001$). In contrast, haemoglobin, haematocrit, and serum creatinine concentrations did not differ significantly between groups. The prevalence of major comorbidities – such as asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure, cerebrovascular disease, diabetes mellitus, liver disease, and renal disease – was comparable between the two groups (all $p > 0.05$). Glucocorticoid treatment was more frequently administered in the eosinopenia group (Table 2). Specifically, glucocorticoids were administered at any time during the study to 18.8% of patients with eosinopenia, compared to 10.4% of those without eosinopenia ($p < 0.0001$). At the time of study inclusion, glucocorticoid use was documented in 8.1% of patients with eosinopenia and 3.7% without eosinopenia ($p = 0.0004$). In addition, 2.8% of patients with eosinopenia and 1.1% without had received glucocorticoids within 24 hours prior to inclusion ($p = 0.0110$).

Eosinopenia (versus non-eosinopenia) correlated with significantly higher CRB-65 ($p < 0.0001$), CURB-65 ($p < 0.0001$), PSI ($p = 0.0001$), IDSA/ATS minor criteria ($p < 0.0001$), and SOFA ($p < 0.0001$). These CAP risk stratification scores of the eosinopenia versus non-eosinopenia group are summarised in Supplementary Table S1.

Table 2. Characteristics of the eosinopenia and non-eosinopenia groups.

Variable	Eosinopenia group (n = 749)	Non-eosinopenia group (n = 1,014)	p-value
Median age in years (25th–75th percentile)	64.00 (49.00–75.00)	61.00 (44.00–73.00)	0.0010
Sample size n (%)	749 (100.0)	1,014 (100.0)	
Male sex, n (%)	460 (61.4)	598 (59.0)	0.5275
Sample size n (%)	749 (100.0)	1,014 (100.0)	
Weight in kg, median (25th–75th percentile)	78.00 (66.00–89.00)	79.00 (66.00–91.00)	0.3042
Sample size n (%)	748 (99.9)	1,014 (100.0)`	
Body mass index in kg/m2, median (25th–75th percentile)	25.86 (22.88–29.70)	26.17 (22.98–30.10)	0.3497
Sample size n (%)	748 (99.9)	1,012 (99.8)	
CRP in mg/L, median, 25th–75th percentile	152.00, 70.50–264.30	124.50, 54.60–217.00	<0.0001
Sample size n (%)	747 (99.7)	1,013 (99.9)	
Procalcitonin in ng/mL, median, 25th–75th percentile	0.70, 0.16–3.70	0.25, 0.10–1.36	<0.0001
Sample size n (%)	390 (52.1)	408 (40.2)	
Leukocytes in × 109/L, median, 25th–75th percentile	12.10, 8.30–17.00	10.70, 8.30–14.23	<0.0001
Sample size n (%)	749 (100.0)	1,014 (100.0)	
Haemoglobin in g/dL, median, 25th–75th percentile	8.32, 7.63–9.00	8.25, 7.63–8.87	0.1388
Sample size n (%)	748 (99.9)	1,014 (100.0)	
Haematocrit in %, median, 25th–75th percentile (%)	0.39, 0.36–0.42	0.39, 0.36–0.42	0.2387
Sample size n (%)	747 (99.7)	1,012 (99.8)	
Creatinine in mg/dL, median, 25th–75th percentile	79.56, 64.53–97.24	77.79, 62.77–97.24	0.1692
Sample size n (%)	669 (89.3)	944 (93.1)	
Asthma, sample size n (%)	54 of 260 (20.8)	78 of 290 (26.9)	0.4821
COPD, sample size n (%)	194 of 260 (74.6)	201 of 293 (68.6)	0.6452
Congestive heart failure, sample size n (%)	101 of 749 (13.5)	107 of 1014 (10.6)	0.3619
Cerebrovascular disease, sample size n (%)	54 of 740 (7.3)	52 of 1009 (5.2)	0.3619
Diabetes mellitus, sample size n (%)	130 of 744 (17.5)	168 of 1013 (16.6)	0.7040
Liver disease, sample size n (%)	20 of 749 (2.7)	21 of 1014 (2.1)	0.6452
Renal disease, sample size n (%)	82 of 748 (11.0)	99 of 1014 (9.8)	0.6452
Glucocorticoids at any time throughout the study, sample size n (%)	141 (18.8)	105 (10.4)	<0.0001
Glucocorticoids at the time of study inclusion, n (%)	61 (8.1)	38 (3.7)	0.0004
Glucocorticoids 24 hours prior to study inclusion, n (%)	21 (2.8)	11 (1.1)	0.0110

COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein.

Clinical outcomes by eosinophil count (≤30/µL versus >30/µL)

Patients with eosinopenia (≤30/µL) experienced significantly worse clinical outcomes compared to those without eosinopenia (>30/µL). The rate of mechanical ventilation was 15.5% in the eosinopenia group versus 7.3% in the non-eosinopenia group ($p < 0.0001$; relative risk [RR], 2.12; 95% confidence interval [CI], 1.61–2.80). Similarly, ICU admission occurred in 23.1% versus 10.9% of patients, respectively ($p < 0.0001$; RR, 2.11; 95% CI, 1.70–2.63). These differences remained consistent at all measured time points (days 1, 5, 10, 15, 30, and 45 after admission; see Figures 1 and 2).

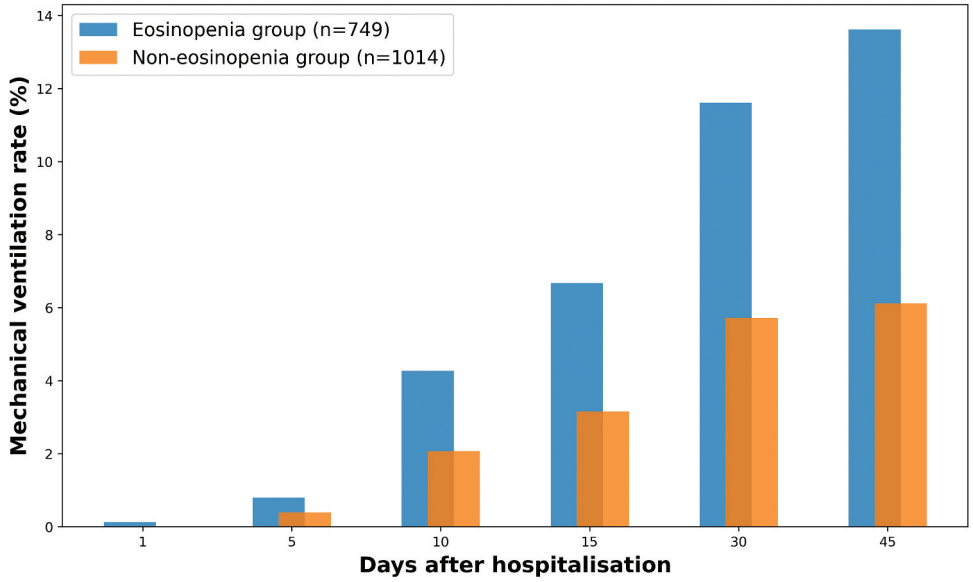

Figure 1. Mechanical ventilation rates in the eosinopenia (≤30/µL) and non-eosinopenia (>30/µL) groups on day 1, 5, 10, 15, 30, and 45 after hospital admission. Total mechanical ventilation rate was 15.5% in the eosinopenia group versus 7.3% in the non-eosinopenia group; RR 2.12; 95% CI 1.61-2.80; $p < 0.0001$ (Fisher's exact test; $n = 1,763$).

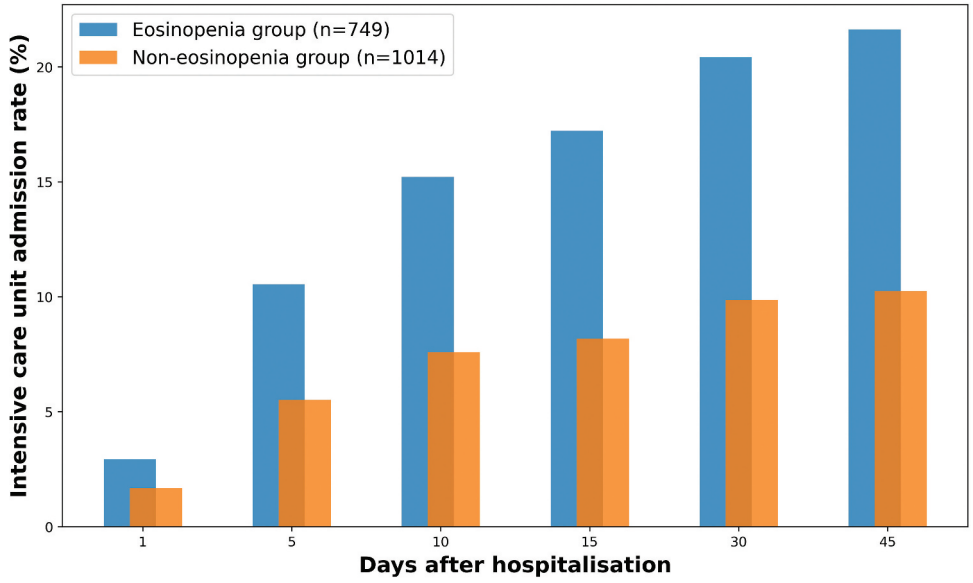

Figure 2. Intensive care unit admission rates (ventilated and non-ventilated patients) in the eosinopenia (≤30/µL) and non-eosinopenia (≤30/µL) groups on day 1, 5, 10, 15, 30, and 45 after hospital admission. Total intensive care admission rate was 23.1% in the eosinopenia group versus 10.9% in the non-eosinopenia group; RR 2.11; 95% CI 1.70-2.63; $p < 0.0001$ (Fisher's exact test; $n = 1,763$).

Table 3. Outcomes in the eosinopenia and non-eosinopenia groups.

Variable	Eosinopenia group ($n = 749$)	Non-eosinopenia group ($n = 1,014$)	p-value
Mechanical ventilation rate, n (%)	116 (15.5)	74 (7.3)	<0.0001 (FET)
Sample size n (%)	749 (100.0)	1,014 (100.0)	
Intensive care admission rate, n (%)	173 (23.1)	111 (10.9)	<0.0001 (FET)
Sample size n (%)	749 (100.0)	1,014 (100.0)	
In-hospital mortality, n (%)	18 (2.4)	17 (1.7)	0.3029 (FET)
Sample size n (%)	749 (100.0)	1,014 (100.0)	
Median length of stay of survivors, days	8.0	7.0	<0.0001 (MWU))
(25th–75th percentile)	(6.0–11.0)	(5.0–9.0)	
Sample size n (%)	728 (97.2)	994 (98.0)	
Median time to in-hospital death, days	12.0	20.0	0.0811 (MWU)
(25th–75th percentile)	(6.5–24.8)	(6.0–60.0)	
Sample size n (%)	18 (2.4)	17 (1.7)	

FET, Fisher's exact test; MWU, Mann-Whitney U test.

Among survivors, the median hospital length of stay was significantly longer in the eosinopenia group (8.0 days [25th–75th percentile, 6.0–11.0]) compared to the non-eosinopenia group (7.0 days [25th–75th percentile, 5.0–9.0]; $p < 0.0001$). A detailed overview of all clinical outcomes stratified by eosinophil count is presented in Table 3.

Discussion

This prospective multicentre cohort study demonstrates that an eosinophil count of ≤30/µL at hospital admission serves as an independent prognostic biomarker for identifying CAP patients at increased risk of respiratory failure, irrespective of systemic glucocorticoid use. Notably, eosinopenia remained significantly associated with poorer clinical outcomes at all analysed time points, emphasising its potential prognostic relevance beyond admission values.

Comparison with existing evidence

Previous studies have consistently associated eosinopenia – commonly defined as an eosinophil count ≤50/µL – with adverse outcomes in CAP. A large multicentre observational study of hospitalised patients with CAP reported that those with eosinophil counts ≤50/µL had higher in-hospital mortality, greater need for mechanical ventilation, increased rates of sepsis, and longer hospital stays compared to those with higher eosinophil counts.[7] Furthermore, among patients with CAP and underlying COPD, eosinopenia (<50/µL) was shown to predict both short- and long-term mortality.[8,9]

Beyond pneumonia, eosinopenia has also been associated with poorer outcomes in older adults with systemic bacterial infections, with eosinophil counts <100/µL independently predicting higher in-hospital mortality.[12]

However, prior studies relied on arbitrarily defined eosinophil count thresholds and did not systematically assess alternative cut-offs. To our knowledge, this is the first study to identify an evidence-based eosinophil count threshold of 30/µL for stratifying the risk of requiring mechanical ventilation in patients with CAP. By analysing eosinophil counts as a continuous variable, we established a clinically relevant cut-off that enhances the utility of eosinopenia in risk prediction. These findings extend the prognostic role of eosinopenia and support its application in early clinical decision-making regarding ventilatory support. However, the area under the curve of 0.63 and sensitivity/specificity values near 60% suggest only moderate discriminative ability; thus, our findings should be interpreted with appropriate caution.

The potential confounding effect of glucocorticoid therapy, which is known to suppress circulating eosinophils, merits particular consideration. Although the role of glucocorticoids in the management of CAP remains debated,[13,14] our findings suggest that the prognostic value of eosinopenia persists regardless of glucocorticoid exposure. While some trials have reported a survival benefit of hydrocortisone in severe CAP requiring intensive care,[15,16] others, such as the study by Meduri et al.[17] found no mortality benefit with prolonged low-dose methylprednisolone. Our results contribute to this ongoing

discussion by demonstrating that eosinopenia remains predictive of respiratory failure even when patients receiving glucocorticoids are excluded, thereby underscoring the robustness of this biomarker.

Clinical implications

This study demonstrates that eosinophil counts provide independent prognostic information in CAP, regardless of the underlying pathogen. As current standard diagnostic procedures do not allow for rapid identification of the causative pathogen at the point of hospital admission, there is a critical need for accessible biomarkers that can inform risk stratification prior to the availability of microbiological results. Our findings suggest that eosinophil counts, a standard component of routine blood tests, may be utilised for this purpose. Integrating eosinophil counts into early clinical risk assessment could enhance patient management by enabling timely identification of individuals at elevated risk for respiratory failure. This, in turn, may support earlier decisions regarding intensified monitoring, ICU transfer, and initiation of ventilatory support, ultimately contributing to improved outcomes in patients with CAP.

Eosinophil counts can vary with age and underlying comorbidities.[18–21] With the aim of minimising age as a confounder, our analysis included age as a covariate in multivariable models. To minimise confounding due to comorbidities, we compared baseline comorbidities between the eosinopenia and non-eosinopenia groups and reported these in Table 2. This comparison did not reveal significant differences in the prevalence of asthma, COPD, congestive heart failure, cerebrovascular disease, diabetes mellitus, liver disease, or renal disease. This suggests that eosinophil count plays a role in CAP outcomes independent of comorbidities in our cohort.

Strengths and limitations

Key strengths of our study include its prospective multicentre design, a large and well-characterised cohort, and the availability of detailed clinical data enabling robust adjustment for relevant confounders, including systemic glucocorticoid therapy. However, certain limitations must be acknowledged. The study population primarily consisted of patients with mild to moderate CAP and the mean age was relatively low; this may be partly due to the need to obtain patient consent prior to enrolment, which can be more challenging in older and frail individuals. Consequently, these factors may limit the applicability of our findings to more severe cases and older patient groups. In-hospital mortality was low, precluding meaningful analysis of 6-month and 1-year mortality rates. In addition, data on the duration of mechanical ventilation, microbiological aetiology, time-to-respiratory failure, vaccination history, cause-specific mortality, and cumulative or total glucocorticoid dose were not collected. Eosinopenia was attributed primarily to the acute inflammatory response to pneumonia; however, a systematic evaluation of other causes of eosinopenia was not feasible.

Conclusions

This prospective multicentre study identifies eosinopenia ≤30/µL at hospital admission as a clinically meaningful and glucocorticoid-independent biomarker for predicting respiratory failure in CAP. Given its availability and ease of measurement, eosinophil count may serve as a valuable tool to enhance early risk stratification and guide timely escalation of care. Validation in broader populations and integration into clinical decision-making frameworks will be essential to confirm its utility and optimise patient management in real-world settings.

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Disclosure statement

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Data availability statement

The data sets used and/or analysed in this study are available on request from the PROGRESS network.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors did not use generative AI.

Human ethics approval declaration

The PROGRESS study is registered at clinicaltrials.gov NCT02782013 (https://clinicaltrials.gov/study/NCT02782013). The study protocol was approved by the ethics committee of the University of Jena (2403–10/08) and by locally responsible ethics committees of all study sites. Informed consent of patients covers initially planned and future research on pneumonia and related disorders.

References

1. WHO. The top 10 causes of death. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. Updated December 9, 2020. Accessed December 7, 2023.
2. Ewig S, Birkner N, Strauss R, et al. New perspectives on community-acquired pneumonia in 388 406 patients. Results from a nationwide mandatory performance measurement programme in healthcare quality. *Thorax*. 2009;64(12):1062–1069. doi: 10.1136/thx.2008.109785.
3. Renaud B, Santin A, Coma E, et al. Association between timing of intensive care unit admission and outcomes for emergency department patients with community-acquired pneumonia. *Crit Care Med*. 2009;37(11):2867–2874. doi: 10.1097/CCM.0b013e3181b02dbb.
4. Phua J, Ngerng WJ, Lim TK. The impact of a delay in intensive care unit admission for community-acquired pneumonia. *Eur Respir J*. 2010;36(4):826–833. doi: 10.1183/09031936.00154209.
5. Restrepo MI, Mortensen EM, Rello J, Brody J, Anzueto A. Late admission to the ICU in patients with community-acquired pneumonia is associated with higher mortality. *Chest*. 2010;137(3):552–557. doi: 10.1378/chest.09-1547.
6. Kolditz M, Ewig S, Klapdor B, et al. Community-acquired pneumonia as medical emergency: predictors of early deterioration. *Thorax*. 2015;70(6):551–558. doi: 10.1136/thoraxjnl-2014-206744.
7. Weckler BC, Pott H, Race A, et al. Eosinopenia as predictor of disease severity in patients with community-acquired pneumonia: an observational study. *Chest*. 2024;166(6):1329–1333. doi: 10.1016/j.chest.2024.05.041. Epub July 5, 2024.
8. Mao Y, Qian Y, Sun X, Li N, Huang H. Eosinopenia predicting long-term mortality in hospitalized acute exacerbation of COPD patients with community-acquired pneumonia-a retrospective analysis. *Int J Chron Obstruct Pulmon Dis*. 2021;16:3551–3559. doi: 10.2147/COPD.S347948.
9. Steer J, Gibson J, Bourke SC. The DECAF score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2012;67(11):970–976. doi: 10.1136/thoraxjnl-2012-202103.
10. Cazzaniga M, Fumagalli LAM, D'angelo L, et al. Eosinopenia is a reliable marker of severe disease and unfavourable outcome in patients with COVID-19 pneumonia. *Int J Clin Pract*. 2021;75(7):e14047. doi: 10.1111/ijcp.14047.
11. Ahnert P, Creutz P, Scholz M, et al. Progress – prospective observational study on hospitalized community acquired pneumonia. *BMC Pulm Med*. 2016;16(1):108. doi: 10.1186/s12890-016-0255-8.
12. Partouche B, Pepin M, de Farcy PM, et al. Persistent eosinopenia is associated with in-hospital mortality among older patients: unexpected prognostic value of a revisited biomarker. *BMC Geriatr*. 2021;21(1):557. doi: 10.1186/s12877-021-02515-0.
13. Vornicu O, Perriens E, Blackman S, et al. Mortality reduction in severe community-acquired pneumonia: key findings from a large randomized controlled trial and their clinical implications. *Ann Transl Med*. 2023;11(11):395. doi: 10.21037/atm-23-1719.
14. Huang J, Guo J, Li H, Huang W, Zhang T. Efficacy and safety of adjunctive corticosteroids therapy for patients with severe community-acquired pneumonia: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2019;98(13):e14636. doi: 10.1097/MD.0000000000014636.
15. Dequin PF, Meziani F, Quenot JP, et al. Hydrocortisone in severe community-acquired pneumonia. *N Engl J Med*. 2023;388(21):1931–1941. doi: 10.1056/NEJMoa2215145.

16. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med*. 2021;384(8):693–704. doi: 10.1056/NEJMoa2021436.
17. Meduri GU, Shih MC, Bridges L, et al. Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. *Intensive Care Med*. 2022;48(8):1009–1023. doi: 10.1007/s00134-022-06684-3.
18. Mathur SK, Schwantes EA, Jarjour NN, Busse WW. Age-related changes in eosinophil function in human subjects. *Chest*. 2008;133(2):412–419. doi: 10.1378/chest.07-2114. PMID:18252914; PMCID:PMC2919352.
19. Pongdee T, Manemann SM, Decker PA, et al. Rethinking blood eosinophil counts: epidemiology, associated chronic diseases, and increased risks of cardiovascular disease. *J Allergy Clin Immunol Glob*. 2022;1(4):233–240. doi: 10.1016/j.jacig.2022.09.001. PMID:36466741; PMCID:PMC9718542.
20. Hartl S, Breyer MK, Burghuber OC, et al. Blood eosinophil count in the general population: typical values and potential confounders. *Eur Respir J*. 2020;55(5):1901874. doi: 10.1183/13993003.01874-2019. PMID:32060069.
21. Abohalaka R, Ercan S, Lehtimäki L, et al. Blood eosinophil reference values and determinants in a representative adult population. *J Allergy Clin Immunol Glob*. 2025;4(2):100449. doi: 10.1016/j.jacig.2025.100449. PMID:40226771; PMCID:PMC11986508.