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COMMENTARY

Role of Eosinopenia as a Prognostic Factor in COVID-19 Patients from Emergency Department During the Second Wave

P. Denoël[1] · K. Brousmiche[1] · D. Castanares-Zapatero[2] · A. Manara[1] · J. C. Yombi[3]

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Dear Editor,

Due to severe acute respiratory syndrome 2 (SARS-CoV-2), the *coronavirus*-19 (COVID-19) pandemic has resulted in a considerable increase in morbidity and mortality worldwide since December 2019. At the admission in emergency department, the initial blood examination can help early detection of patients that are at high risk of death.

In this context, many biomarkers have been correlated to the risk of mortality. Based on these, a lot of scores are coming for scoring the mortality of SARS-CoV-2, but few of them are based on eosinopenia [1]. However, eosinopenia, when associated with other factors, gives interesting results [2].

Eosinophils are granulocytes that still have potent pro-inflammatory effects and participate in immunoregulation and in host defense against many diseases including bacterial and viral infections. Eosinopenia is defined as a reduced number of circulating eosinophils in blood. A correlation has been reported between eosinopenia and infection with SARS-CoV-2 in some studies [3]. The physiopathology of eosinopenia in SARS-CoV-2 infection is not completely understood. It seems to be multifactorial. Presumed factors are, e.g., reduced production and reduced release of cells from the bone marrow and increased apoptosis induced by type 1 interferons (IFNs) that are released during the acute infection. Blood level of eosinophils is easy to obtain and is an early and frequent biomarker in COVID-19 patients [4].

This study investigates the correlation of eosinopenia (<20 cells/mm^3) at admission with 30-day inhospital mortality from COVID-19 patients admitted in the emergency department (ED) in a large nonacademic hospital in Belgium. It is a retrospective observational, non-interventional, monocentric study during a 4-month period (September 2020 to December 2020). The study included every patient over the age of 18 who was admitted in the ED with a positive SARS-CoV-2 PCR on nasopharyngeal swab. A total of 411 patients were preselected, and 379 were retained for analysis, the remaining 32 patients being excluded due to a lack of data.

The median age was 70 (18–101 years old), and there were 52.5% of men. We found 63.93% of patients with eosinopenia, i.e., a cell count less than 20 cells/mm^3. The 30-day inhospital mortality rate was 24% (90/379). In the multivariate analysis, the following markers were associated with 30-day inhospital mortality (Table 1): eosinopenia ($aOR = 2.27$; 95% *CI*: 1.09–4.73, $p = 0.028$), cardiovascular diseases ($aOR = 2.04$; 95% *CI*: 1.02–4.07, $p = 0.043$), dementia ($aOR = 4.44$; 95% *CI*: 1.80–10.90, $p = 0.001$), intubation ($aOR = 6.61$; 95% *CI*: 1.98–22.03, $p = 0.002$), and neutrophil-to-lymphocyte ratio (NLR) ($aOR = 1.05$; 95% *CI*: 1.01–1.09, $p = 0.01$). The ROC curve assessing the eosinopenia and 30-day inhospital mortality shows an area under the curve 0.574.

Eosinopenia was an independent risk factor of 30-day inhospital mortality in COVID-19 patients hospitalized from our ED in this study. The other independent risk factors for 30-day inhospital mortality we found are age, dementia, cardiovascular diseases, intubation, and NLR. The combination of different independents factors from the ED can help in achieving a better risk scoring of the COVID-19 patient, hence a more appropriate management. Eosinopenia can be a part of it.

This article is part of the Topical Collection on *Covid-19*

✉ P. Denoël
p.denoel@europehospitals.be

1 Emergency Department, Cliniques de l'Europe, Brussels, Belgium

2 Intensive Care Unit, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium

3 Infectious Diseases and Internal Medicine Department, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium

Table 1 Descriptive analysis of the cohort

Variable	Subvariable	Total	Univariate analysis		Multivariate analysis	
			OR (95% *CI*)	*p*-value	aOR (95% *CI*)	*p*-Value
Mean age		(70.67 years old)	1.06 (1.040–1.080)	< 0.001	1.055 (1.023–1.089)	< 0.001
Sex (%)	Female	180 (47.5%)	0.559 (0.344–0.910)	0.019	0.266 (0.132–0.536)	< 0.001
	Male	199 (52.5%)				
Comorbidities						
Cardiovascular background, *n* (%)		134 (35.4%)	2.868 (1.764–4.663)	< 0.001	2.041 (1.023–4.075)	0.043
Dementia, *n* (%)		50 (13.2%)	3.678 (1.985–6.817)	< 0.001	4.437 (1.806–10.903)	< 0.001
Diabetes, *n* (%)		94 (24.8%)	1.138 (0.664–1.951)	0.639		
Neurologic, *n* (%)		13 (3.4%)	0.962 (0.259–3.574)	0.954		
Cancer, *n* (%)		61 (16.1%)	1.574 (0.861–2.875)	0.140		
Hypertension, *n* (%)		172 (45.5%)	1.009 (0.628–1.623)	0.970		
Renal failure, *n* (%)		42 (11.1%)	1.941 (0.982–3.836)	0.056		
Pulmonary disease, *n* (%)		50 (13.2%)	0.672 (0.313–1.443)	0.308		
Symptoms						
Fever, *n* (%)		158 (41.7%)				
Respiratory symptoms, *n* (%)		227 (59.9%)				
Gastrointestinal symptoms, *n* (%)		61 (16.1%)				
Cold symptoms, *n* (%)		115 (30.3%)				
Anosmia, *n* (%)		21 (5.5%)				
Clinical parameters						
Oxygen saturation (%)		340 (89.7%)	For spO2 < 92% 0.947 (0.906–0.989)	0.014		
Systolic blood pressure (%)		351 (92.6%)	1.000 (0.999–1.001)	0.420		
Diastolic blood pressure(%)		349 (92.1%)	0.987 (0973–1.000)	0.052		
Respiratory rate (/min)		251 (66.22)	For RR > 20/min 1.022 (0.994–1.051)	0.119		
Paramedical examinations						
PaO_2 in ED		275	For pa O2 < 60 mmhg 0.992 (0.973–1.012)	0.427		
CRP in ED		375	For CRP > 50 mg/L 1.005 (1.002–1.007)	< 0.001		
Eosinophil count Eosinopenia < 20 mm^3		378 241	For eosinopenia < 20 mm^3 1.995 (1.167–3.412)	0.012	For eosinopenia < 20 mm^3 2.274 (1.093–4.731)	0.028
Neutro/lymphocytes rate		378	For N/L > 6 1.083 (1.049–1.117)	< 0.001	1.051 (1.012–1.091)	0.010
Pneumonia on imaging		264	5.059 (2.246–11.397)	< 0.001	5.563 (1.733–17.860)	0.004
Intubation		26 (6.9%)	8.689 (3.231–23.367)	< 0.001	6.611 (1.983–22.034)	0.002

Legend: *aOR*, adjusted odds ratio; *CRP*, C-reactive protein; *ED*, emergency department; *OR*, odds ratio; *PaO2*, arterial partial oxygen pressure

In a study of 107 consecutive patients with pneumonia and a positive COVID-19 nasopharyngeal swab, Cazzaniga et al. [5] found that 75 patients had undetectable eosinophil count (absolute eosinopenia). Compared with patients without absolute eosinopenia, patients with absolute eosinopenia had more frequent need of intensive respiratory treatment (49.3% vs 13.3%, $P < 0.001$), higher mortality (30.6% vs 6.2%, P 0.006), and lower rate of hospital discharge (28% vs 65.6%, $P < 0.001$). They concluded that absolute eosinopenia is associated with worse clinical outcomes in patients with COVID-19 pneumonia and might be used as a marker to discriminate patients with unfavorable prognosis.

In our study, other blood tests, like the NLR, were also predictive of a higher risk of 30-day mortality. Khourssaji et al. [4] also reported that high values of CRP, NLR, D-dimers, ferritin, and lymphopenia and eosinopenia were consistently associated with a higher risk and were good markers for risk stratification.

The limitations of our study are the following: it is a retrospective and monocentric study; it is based only on eosinopenia we cannot completely predict in the course of

patients, because other factors influence the disease outcomes such as age and comorbidities. The variables chosen were those which were both of interest for the study and were significant. The others were not retained. First, eosinophils is available worldwide and is easy to obtain. Secondly, our study is one of the largest one performed in ED in which the impact of eosinopenia on mortality from COVID-19 patients has been analyzed during the second wave. The cutoff < 20 °C/mm^3 is due to the choice of our laboratory for the definition of eosinopenia in this range of patients. The same cutoff is taken in the other studies [2].

Finally, although the ROC curve does not give the expected result, it is essential in the description of this study and should be studied with a larger cohort.

This study suggests the possibility to use eosinophil cell count (eosinopenia < 20 °C/mm^3) at emergency admission as a risk marker of 30-day inhospital mortality from COVID-19 patients. This study has been performed in a specific hospitalized population from ED, and future studies should be considered in order to confirm the actual interest of eosinopenia as a predictive factor, possibly in a predictive score of mortality.

Author Contribution Denoël P. had the idea for the project and corrects the paper. Brousmiche K. makes the paper, with references, corrects it, and publishes it. Castanares-Zapatero D. makes the statistics. Manara A. corrects the paper. Yombi J. C. has the idea, makes the paper, and corrects it.

Data Availability Only one request.

Code Availability Not applicable.

Declarations

Ethics Approval Approved.

Consent to Participate Retrospective study not applicable.

Consent for Publication Retrospective study not applicable.

Conflict of Interest The authors declare no competing interests.

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