Association between low eosinophil count and mortality in SARS-COV-2 infection on the 70+, a discussed observation

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Research Article
Abstract

**Background:** Biological COVID-19 abnormalities are varied (lymphopenia, high levels of blood inflammatory markers, ...). Regarding physiological immune responses, eosinophils were for a long time thought to be mainly against extra-cellular pathogen like helminthes. It has recently been pointed out that they appear to play a part in recognition of virus and to have the capacity to perform direct action against viruses. This study aimed to seek for an association between eosinophils count < 10 /mm3 and mortality in an older adults suffering from COVID-19 hospitalized in a specific geriatric ward.

**Methods:** This observational retrospective study was conducted in a French geriatric ward from March 17 to April 18, 2020. All 118 patients hospitalized for COVID-19 over 70 yo in acute stay care were enrolled. Patients with a treatment or a condition which could interfere with eosinophil count were excluded.

**Results:** No statistical difference was found between surviving or deceased patient regarding age (mean age (SD): 87 years (7)) and sex (34% of males). Differences for the most frequent acute events were statically different: Quick Sepsis-related Organ Failure Assessment (qSOFA) score was ≥ 2 at admission for 23% in the survivor group vs 72% in the deceased (p < .001); acute kidney injury concerned 17% of the survivors vs. 69% of the decease (p< .001). Eosinophil count < 10/mm3 was significantly associated with mortality (OR (95% CI)) = 3.54 (1.23-11.4) after adjustment on age, gender, and activity of daily living.

**Conclusion:** Low eosinophil count (< 10/mm3) seems to be associated with mortality on older adults. Due to the specific physiological ageing process of the immune system, this calls to explore more globally the impact of inflammaging and immunosenescence on SARS-CoV-2 infection in this population.

Introduction

SARS-COV-2 outbreak, stated in winter 2020 as a public health emergency of international concerned by the World Health Organization (WHO) disrupted societies, health systems and scientific paradigms: everything needed to be learned. Indeed, due to its large spreading and lethality, the understanding of its physiopathology as much as finding prognostic factors are needed for health system to be re-organized and clinician to make decisions. It has affected every country, resulting in more than 238 million identified cases with 4 million confirmed deaths since December 2019 (1). In this context, our elders (a world growing population) seem more vulnerable: since the first of March, 73% of the deceased were 75 years old or more in France (2).

Age has indeed been described to be a major independent prognostic factor, as hypertension, diabetes and obesity (3–7). Of note, our deceased in a geriatric COVID-19 ward this fall were highly disabled as shown by Zerah and al (8). Their activity of daily living (ADL) - scored over 6 which marks no disability (9) – was significantly associated with mortality: ADL ≤ 3 had an OR of 1.84 (1.25–2.70) on the multivariate analysis. However, the age adjusted Charlson comorbidity index (10) did not seem to be a significant prognostic variable on mortality status: median (IQR) were 7 (6–9) vs 7 (6–8) p=0.28.
Biological COVID-19 abnormalities include lymphopenia, increased levels of blood inflammatory markers (such as C-reactive protein (CRP), ferritin, ...) and a high lactate dehydrogenase (LDH) blood level (11). Regarding physiological aspect, immune responses are usually classified in three types against pathogens: type 1 against intra-cellular pathogen including viruses, type 2 against extra-cellular pathogen like helminthes and type 3 against extra-cellular pathogen like bacteria and fungus (12). Eosinophils were for a long time included in the type 2 response and explored for their implication in allergic or pulmonary diseases (13). Their role appears to be wider as they have been linked to immune response conferring host protection against fungi, bacteria, and viruses. They seem to be able to play a part in recognition of virus and to have the capacity to perform direct action against viruses (13).

However, literature between eosinophils and infectious diseases – helminthes apart – appears to be scarce. One study found that eosinophil count under 40/mm3 with elevated white cell count (over 10,000/mm3) was associated with bacterial infectious diseases (14,15). Another study found that eosinophils < 10/mm³ alone or in association with elevated white blood cell count or high CRP blood level was strongly associated with sepsis (specificity 94-98 %) in an emergency department (16). A third study found that eosinophils < 40/mm3 was a strong (all-cause) mortality predictor (Hazard Ratio 1.85 (95%CI 1.01-3.42), p = 0.046) in intensive care unit (17). Along with these observations, studies on SARS-COV-2 found that low count seemed to be correlated with the prognosis (18–21). Interestingly, eosinophil levels increased in patients prior discharge, suggesting that following their rate might help to monitor betterment (22). Although it remains unclear, low eosinophil count for some authors involves inhibition of eosinophil life cycle, apoptosis may be induced by interferon type 1 during acute infection and eosinophil consumption through eosinophil antiviral actions(13).

In this way, low eosinophil count could be a prognosis marker for mortality (17,23,24); however, none of these reports included geriatric patients (over 75 y.o with significant comorbidities and disability).

Thus, this study analyzed the association between low eosinophil count (< 10 /mm3) and mortality in older adults hospitalized in a specific geriatric COVID-19 ward.

**Materials And Methods**

**Study Design, Setting, and Participants**

This monocentric retrospective cohort was an ancillary study of the Zerah and al cohort which took place from March 13 to April 15 2020 (8). Informed consent was obtained for all participants and this study was approved by the University Hospital of Paris research committee on April 17, 2020 and by the institutional ethics board of Sorbonne University on May 11, 2020 (2020-CER-2020-43). This report follows the STROBE recommendations.

Inclusion criteria were: at least age 70 years old and hospitalization in a geriatric ward for COVID-19. Non-inclusion criteria were conditions or medications that might modify eosinophil count:
immunosuppression (HIV with CD4 < 200/ mm3), chronic corticosteroid use, asthma, chemotherapy or immunosuppressive agents, documented lymphoproliferative or myeloproliferative disorders and documented parasitic diseases.

The diagnosis of COVID-19 was confirmed by a nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2, according to the WHO guidance (25).

Data Collection Methods and Data Management

Patients’ medical records were reviewed and analyzed by trained physicians. We included baseline characteristics before COVID-19-19: age, gender, community or nursing home residence, previous medical history, and chronic medications. Recorded comorbidities were: atrial fibrillation, active cancer, dementia, depression, diabetes, congestive heart failure, coronary artery disease, thromboembolic disease, hemiplegia, stroke, Chronic Obstructive Pulmonary Syndrome (COPD), peripheral arterial obstructive disease, hypertension, Parkinson disease, chronic kidney disease. Severity was assessed with the Charlson's index (10) and functional status was assessed by the Activities of Daily Living (ADL) scale (6 basic human functions: bathing, dressing, toileting, transfer, continence, and feeding; 1 point for each function (9)). ADL was categorized in a binary variable: ADL < 3. According to French health authority (Haute Autorité de Santé), eosinophils count respectively for male and female over 65 y.o is 50/mm3 - 690/mm3; 40/mm3 – 450/mm3 (2.5 percentile – 97.5 percentile)(26). Due to the very low eosinophils count in this cohort, cut-off for low eosinophil count was set to < 10/mm3 because it has been associated with poor outcome during sepsis and defined absolute eosinopenia (16).

Acute events were recorded: atrial fibrillation, heart failure, pulmonary edema, disorders of consciousness defined by Glasgow score < 14, thromboembolic or hemorrhagic event, acute kidney failure identified according to the Kidney Disease Improving Global Outcomes (KDIGO) definition (27), fecal impaction, acute urinary retention, pressure ulcer.

Quick Sepsis-related Organ Failure Assessment ≥ 2 (qSOFA), defined by a range 0-3, with 1 point each for systolic hypotension (≤ 100 mmHg), tachypnea (≥ 22/min) or altered consciousness (Glasgow coma score < 14) was recorded (28). Biological data during infection were also collected: white blood cell count, neutrophil count, eosinophil count, lymphocytes count, platelets count, hemoglobin level, presence of liver injury (aspartate aminotransferase or alanine aminotransferase ≥ 2 times normal level) and cholestasis with alkaline phosphatase or gamma-glutamyltransferase ≥ 2 times the upper limit of normal. Data at discharge were also reported: vital status (alive or dead), length of stay and discharge location (home; nursing home; long term rehabilitation center or other).

Statistical analysis
As we included all patients from the center, no a priori power calculation was done. Normality of variable was assessed by a graphical representation of their distribution. Data are presented with mean and standard deviation (SD) for continuous variables and count (percentage) for categorical variables. T-tests were used for continuous variables and chi-squared tests or Fisher's exact tests for categorical variables. Patient characteristics are described overall and according to mortality status during the stay in the acute geriatric stay.

Missing values represented overall less than 8% of all of the data and 4% for the variable used in the multivariate analysis. Thus, no imputation of the missing data was performed.

We performed exploratory analysis in order to assess for other associated factors with mortality and their correlation by a focused principal components analysis.

We performed a logistic regression with adjustment for age, sex and ADL > 3. ADL was chosen because it was a significant factor in the main study and is a relevant geriatric variable. No stepwise was performed due to the limited power and the number of missing data.

Analyses were performed with R V4.0.0.

Results

One hundred and eighteen patients were included during the study period. The mean (SD) length of stay was 12.3 (7.4) days with a statistical difference between survivors (13.5 (7.0) days) and deceased (9 (7.5) days). 32 (27%) patients have died during their stay in our acute COVID-19 ward. As for the survivors, 42 (35.6%) patients were transferred to a rehabilitation ward, 33 (28.0%) patients returned home and 5 (4.2%) were transferred to another ward such as palliative care.

Demographic and clinical data of the population are presented in table 1. No statistical difference was found between surviving or deceased patient regarding age and sex (mean age (SD) was 87 years (7); p = 0.54)) and 40 (34%) were male (p=0.07). The age adjusted Charlson comorbidity index was high in both groups with a trend for a higher score for the deceased (mean (SD) = 4.7 (2.7) vs 5.7 (2.9), p = 0.10), as well as a more frequent ADL score < 3 (47 (55%) for survivors vs. 23 (72%), p=0.06).

Table 1: Baseline characteristics and acute events
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Survivor</th>
<th>Deceased</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 118</td>
<td></td>
<td>n = 86 (73%)</td>
<td>n = 32 (27%)</td>
<td></td>
</tr>
<tr>
<td><strong>Socio-demographic data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)*</td>
<td>87.0 (7)</td>
<td>86.7 (6.2)</td>
<td>87.6 (6.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>40 (34.0)</td>
<td>25 (29.1)</td>
<td>15 (47.0)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Comorbidities, mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Charlson comorbidity Index</td>
<td>5.0 (2.8)</td>
<td>4.7 (2.7)</td>
<td>5.7 (2.9)</td>
<td>0.10</td>
</tr>
<tr>
<td>Number of treatments</td>
<td>7.3 (3.5)</td>
<td>7.3 (3.6)</td>
<td>7.3 (3.2)</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Comorbidities, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>43 (36.4)</td>
<td>27 (31.4)</td>
<td>16 (50.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Active cancer</td>
<td>14 (11.9)</td>
<td>11 (12.8)</td>
<td>3 (9.4)</td>
<td>0.76</td>
</tr>
<tr>
<td>Dementia</td>
<td>97 (82.2)</td>
<td>69 (80.2)</td>
<td>28 (87.5)</td>
<td>0.36</td>
</tr>
<tr>
<td>Depression</td>
<td>66 (55.9)</td>
<td>51 (59.3)</td>
<td>15 (46.9)</td>
<td>0.23</td>
</tr>
<tr>
<td>Diabetes</td>
<td>35 (29.7)</td>
<td>24 (27.9)</td>
<td>11 (34.4)</td>
<td>0.49</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>39 (33.1)</td>
<td>25 (29.1)</td>
<td>14 (43.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>32 (27.1)</td>
<td>21 (24.4)</td>
<td>11 (34.4)</td>
<td>0.28</td>
</tr>
<tr>
<td>Thromboembolic disease</td>
<td>17 (14.4)</td>
<td>13 (15.1)</td>
<td>4 (12.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>10 (8.5)</td>
<td>6 (7.0)</td>
<td>4 (12.5)</td>
<td>0.46</td>
</tr>
<tr>
<td>Stroke</td>
<td>32 (27.1)</td>
<td>16 (18.6)</td>
<td>16 (50)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>COPD</td>
<td>14 (11.9)</td>
<td>10 (11.6)</td>
<td>4 (12.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Peripheral arterial obstructive disease</td>
<td>14 (11.9)</td>
<td>7 (8.1)</td>
<td>7 (22)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>85 (72)</td>
<td>61 (71)</td>
<td>24 (75)</td>
<td>0.66</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>7 (5.9)</td>
<td>7 (8.1)</td>
<td>0 (0)</td>
<td>0.19</td>
</tr>
<tr>
<td>Chronical kidney disease</td>
<td>32 (27.1)</td>
<td>19 (22.1)</td>
<td>13 (40.6)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Autonomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living in nursing home, n (%)</td>
<td>73 (61.9)</td>
<td>50 (58.1)</td>
<td>23 (71.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>ADL&lt;3, n (%)</td>
<td>70 (59.3)</td>
<td>47 (54.7)</td>
<td>23 (71.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>23.1 (4.9)</td>
<td>22.9 (4.7)</td>
<td>23.8 (5.8)</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>Acute events, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Characteristics</td>
<td>Total</td>
<td>Survivor</td>
<td>Deceased</td>
<td>p</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>--------</td>
<td>------------</td>
<td>-----------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>n = 118</td>
<td>n = 86 (73%)</td>
<td>n = 32 (27%)</td>
<td></td>
</tr>
<tr>
<td>Acute atrial fibrillation</td>
<td>4 (3.4)</td>
<td>4 (4.7)</td>
<td>0 (0)</td>
<td>0.57</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>6 (5.1)</td>
<td>3 (3.5)</td>
<td>3 (9.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>Acute coronary event</td>
<td>1 (0.8)</td>
<td>1 (1.2)</td>
<td>0 (0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Glasgow score &lt; 15</td>
<td>39 (33.1)</td>
<td>12 (14.0)</td>
<td>27 (84.4)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Thromboembolic event</td>
<td>1 (0.8)</td>
<td>1 (1.2)</td>
<td>0 (0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Hemorrhagic event</td>
<td>5 (4.2)</td>
<td>4 (4.7)</td>
<td>1 (3.1)</td>
<td>0.99</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>37 (31.4)</td>
<td>15 (17.4)</td>
<td>22 (68.8)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>qSOFA ≥ 2</td>
<td>44 (37.3)</td>
<td>20 (24.4)</td>
<td>23 (71.9)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Oxygen n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt; .001</td>
</tr>
<tr>
<td>None</td>
<td>54 (45.8)</td>
<td>48 (55.8)</td>
<td>6 (18.8)</td>
<td></td>
</tr>
<tr>
<td>&lt; 9 l/min</td>
<td>52 (44.1)</td>
<td>37 (43.0)</td>
<td>15 (46.9)</td>
<td></td>
</tr>
<tr>
<td>9-15 l/min</td>
<td>12 (10.2)</td>
<td>1 (1.2)</td>
<td>11 (34.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Specific treatments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics introduction, n (%)</td>
<td>75 (63.6)</td>
<td>52 (60.5)</td>
<td>23 (71.9)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*SD : Standard deviation

Abbreviations: ADL: Activities of Daily Living; BMI: Body Mass Index; qSOFA: quick Sequential Organ Failure Assessment, Acute kidney injury: identified according to the Kidney Disease Improving Global Outcomes (KDIGO) definition.

QSOFA score ≥ 2 at admission and acute kidney injury were significantly more frequent in the deceased group than in the survivor group (23 (72%) vs. 20 (23%), p < .001) and 22 (69%) vs. 15 (17%), p < .001 respectively).

Biological data are described in table 2. Regarding blood cells count, eosinophil count < 10/mm3, was more frequent in the deceased group than in the survivor group (36 patients (42%) vs. 17 patients (53%); p =0.008).

Table 2: Laboratory findings
<table>
<thead>
<tr>
<th>Biological characteristics</th>
<th>Total</th>
<th>Survivor</th>
<th>Deceased</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>n = 118</td>
<td>n = 86 (73%)</td>
<td>n = 32 (27%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max Hemoglobin (g/dL)</td>
<td>13.2 (1.80)</td>
<td>13.2 (1.80)</td>
<td>13.4 (2.00)</td>
<td>0.67</td>
</tr>
<tr>
<td>Min Hemoglobin (g/dL)</td>
<td>11.4 (1.70)</td>
<td>11.3 (1.70)</td>
<td>11.6 (1.70)</td>
<td>0.53</td>
</tr>
<tr>
<td>Max leukocyte count (mm3)</td>
<td>7943 (2979)</td>
<td>7410 (2699)</td>
<td>9830 (3209)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Min leukocyte count (/mm3)</td>
<td>4704 (1925)</td>
<td>4320 (1172)</td>
<td>6063 (3147)</td>
<td>0.01</td>
</tr>
<tr>
<td>Max neutrophil count (/mm3)</td>
<td>5629 (2688)</td>
<td>5025 (2249)</td>
<td>7934 (3019)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Min neutrophil count (/mm3)</td>
<td>3043 (1790)</td>
<td>2646 (1066)</td>
<td>4495 (2887)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Max eosinophil count (/mm3)</td>
<td>150 (152)</td>
<td>169 (160)</td>
<td>79 (86)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Min eosinophil count (/mm3)</td>
<td>31(58)</td>
<td>36(62)</td>
<td>13(36)</td>
<td>0.03</td>
</tr>
<tr>
<td>Max lymphocyte (/mm3)</td>
<td>1496 (689)</td>
<td>1521 (655)</td>
<td>1400 (816)</td>
<td>0.53</td>
</tr>
<tr>
<td>Min lymphocyte count (/mm3)</td>
<td>894 (512)</td>
<td>920 (494)</td>
<td>803 (570)</td>
<td>0.37</td>
</tr>
<tr>
<td>Max platelet count (/mm3)</td>
<td>313 898 (108 902)</td>
<td>327 529 (108 814)</td>
<td>263 522 (95 400)</td>
<td>0.01</td>
</tr>
<tr>
<td>Min platelet count (/mm3)</td>
<td>194 000 (62 931)</td>
<td>198 518 (58 771)</td>
<td>178 000 (75 095)</td>
<td>0.23</td>
</tr>
<tr>
<td>Max CRP (/mm3)</td>
<td>110.8 (87.0)</td>
<td>205.1 (85.5)</td>
<td>84.2 (66.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Liver Cytolysis, n (%)</td>
<td>9 (7.60)</td>
<td>4 (4.70)</td>
<td>5 (15.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cholestasis, n (%)</td>
<td>11 (9.30)</td>
<td>5 (5.80)</td>
<td>6 (18.8)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

The multivariate analysis shows that low eosinophil count was associated with an OR of 3.54 (1.23-11.4) after adjustment for age, sex and ADL < 3 (figure 1).

Figure 1: Multivariate analysis (deceased status adjusted on age, sex, eosinophil count and functional status), Forest Plot

OR (95% CI): Age: 1.0 (0.92-1.10), Sex (ref = F): 2.50 (0.80-7.92), Eosinophil count: 3.54 (1.23-11.4), ADL < 3 (ref = No): 0.36 (0.09-1.17)

Discussion
This study tends to show that eosinophils count $< 10$/mm$^3$ was associated with mortality: OR (95% CI) 3.54 (1.23-11.4) after adjustment for age, gender, and disability (i.e., ADL $< 3$) older patients suffering from COVID-19. At first glance, these results seem to be in line with literature (29–33) where low eosinophil count is associated with poorer prognostic and conversely, a better prognosis when subjects present eosinophilia due to asthma (34,35).

However, this result does not seem consistent with Lucas and al (12). In this longitudinal analysis of immunological events in moderate and severe COVID-19 on 135 patients, compared to 108 healthy volunteers, they found that severe cases were associated with a higher eosinophil rate compare to moderate and control cases: $p = 0.016$ for severe cases vs moderate cases and $p < 0.01$ for severe cases vs. controls. In order to discuss this difference between our results and this immunology mapping, some points need to be clarified.

First, in the Lucas and al. cohort, participants were much younger (mean age (SD) = 63 (17)) than our participants (mean age (SD) of 87 (7) years old (6)). Immunosenescence and inflammaging, a chronic inflammatory state observed in the elderly where there is an elevation of pro-inflammatory mediators such as including interleukin-1, beta interleukin-6 and tumor necrosis factor alpha (36) might be involved in the differences observed. This chronic pathological state may be worsened during the “cytokine storm” in which it has been found a significant elevation of the same factors on younger subjects and results in an immunodeficiency (37). However, even though inflammation remains the main hypothesis, it is interesting to notice that unlike other cohort (38) in which the cardiovascular burden (hypertension, congestive cardiac heart failure, atrial fibrillation) has been highlighted to be a major prognostic factor were not statistically associated with mortality. This may be explained by the much higher prevalence of these conditions in our study.

Secondly, as exposed in the introduction, eosinophils are likely to be involved during immune responses against viruses. However, it has been described that during an acute inflammation state caused by bacterial infection, there is a drop of circulating eosinophils due to accumulation of eosinophils at the periphery of the inflammatory site, and an inhibition of egress of eosinophils from the bone marrow which leads to inhibition of eosinopoiesis(39)). Furthermore geriatric patients may be more vulnerable to bacterial secondary infection such as aspiration pneumonia due to deglutition disorder, are highly prevalent in geriatric population (44% in geriatric acute care) (40); the observed low eosinophil count in this study might therefore be in part explained by bacterial secondary infections. Moreover, even though recruitment in lungs tissue does not seem to appear during a COVID-19 infection (41), it has been suggested by Lindsley and al (42) that these low eosinophil count could be the result of a similar mechanism than the one described during bacterial infection. Thus, low eosinophil count might be a sign of host exhaustion imputable to the elimination of COVID-19 virus (43).

Finally, we can notice the significant proportion of Chronical kidney disease and AKI in the deceased group: 40.6% vs 22.1%; $p = 0.027$ and 69% vs 17%, $p < .001$ respectively. This point is relevant because as we can find significant link between eosinophilia (44) and kidney diseases, it seems that low eosinophil
count during SARS-CoV-2 infection might overtake the mechanism that leads to eosinophilia when suffering from kidney injury.

To conclude, one could make the assumption that a poor prognostic of a SARS-CoV-2 infection can, among other factors, be the result of a lack of the antiviral activity and immunomodulation provided by the eosinophils. Hence, it might be a marker to start specific therapy such as antiviral or immunomodulator.

We recognize that the non-inclusion of neutrophils in the multivariate analysis can be a major limit. However, due the conception of the main study, the contemporaneous rate of neutrophils was not accounted for when the minimum of eosinophil count was recorded. Thus, neutrophils’ maximum and minimum were not useable in the same model as the lowest eosinophil count.

We acknowledge that the retrospective and monocentric nature of this study limit the scope of the study and preclude any causal inference of the results.

Finally, the small sample size induced an important lack of power, which only enable a limited multivariate analysis.

**Conclusions And Implications**

Although this study suffers some limitations, this result if confirmed in other study, gives an additional element for clinician to predict the outcome of a SARS-COV-2 infection on geriatric patients. Indeed, eosinophils count< 10/mm$^3$ tends to be associated with mortality on older adults. Due to the specific physiological ageing process of the immune system, this calls explore more globally the impact of inflammaging and immunosenescence on SARS-CoV-2 infection in this population.

**Declarations**

**Ethics approval and consent to participate:** This study approved by the research committee of the University Hospital of Paris on April 17, 2020 and by the institutional ethics board of Sorbonne University on May 11th, 2020 (2020-CER-2020-43). Informed consent was obtained for all participants. This study is in line with article L1121-1 of French Public Health and French data protection authority.

**Consent for publication:** Not applicable.

**Competing interests:** None of the authors have conflicts of interest to disclose and meet the criteria for authorship as stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals ICMJE criteria.

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• Study concept and design: Duron Emmanuelle, Baudouin Edouard
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• Analysis and interpretation of data: Baudouin Edouard, Vidal Jean-Sébastien
• Drafting of the manuscript: Kosowski Jill, Baudouin Edouard
• Critical revision of the manuscript for important intellectual content: Mésinèle Léa, Pujol Tom, Brunetti Nicoletta, Colas Marion, Neiss Marie, Simon Pauline, Trivalle Christophe, Tiramine Soraya, Laraaj Fahd, Vetillard Anne-Laure, Houenou-Quenum Nadège, Souques Cécile, Verdier Sébastien, Houdre Julie, Sorrel-Dejerine Adrien, Sanchez-Tamayo Jorge, Vidal Jean-Sébastien, Collarino Rocco, Guichardon Magali, Jean-Emmanuel Kahn.

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Availability of data and materials: The datasets used during the current study is available from the corresponding author on reasonable request

**References**


**Figures**

![Forest Plot OR (95% CI): Age: 1.0 (0.92-1.10), Sex (ref = F): 2.50 (0.80-7.92), Eosinophil count: 3.54 (1.23-11.4), ADL < 3 (ref = No): 0.36 (0.09-1.17)](image)

**Figure 1**

Multivariate analysis (deceased status adjusted on age, sex, eosinophil count and functional status), Forest Plot OR (95% CI): Age: 1.0 (0.92-1.10), Sex (ref = F): 2.50 (0.80-7.92), Eosinophil count: 3.54 (1.23-11.4), ADL < 3 (ref = No): 0.36 (0.09-1.17)