Circulating nucleosomes are markers of NETosis and correlate with SOFA scores in sepsis

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Background

Septic shock and COVID-19 involve an excessive inflammatory reaction and release of Neutrophil extracellular traps (NETs). The inflammatory reaction in critical COVID-19 and septic shock patients differs on admission to ICU [1] but no direct comparison of NETosis biomarkers has been described.

Our aim was to evaluate NETosis biomarkers in these conditions and compare the results with SOFA (sequential organ failure assessment) and APACHE-II (acute physiology and chronic health evaluation) scores.

Materials and Methods

Study population: 22 patients with critical COVID-19 admitted to the ICU for moderate or severe acute respiratory distress syndrome (ARDS) due to SARS-CoV-2 infection were included within five days of admission. ARDS was diagnosed according to the Berlin definition, and SARS-CoV-2 infection was demonstrated by real-time reverse transcription PCR on nasopharyngeal swabs. **46** patients with septic shock (defined according to the Sepsis-3 definition) admitted to the ICU were included within two days of admission. **48** control patients with matched age, gender, and comorbidities were recruited at a central laboratory consultation.

Blood biomarkers assays. Nucleosome containing histone H3.1 (Nu.Q® H3.1) or citrullinated histone H3R8 (Nu.Cit-H3R8) were measured using the Nu.Q® H3.1 and Nu.Q® H3R8Cit ELISA assays from Volition (Belgian Volition). Neutrophil elastase (NE) and myeloperoxidase (MPO) were measured using the Human Neutrophil Elastase/ELA2 DuoSet ELISA and the Human Myeloperoxidase Quantikine ELISA Kit (R&D systems).

References

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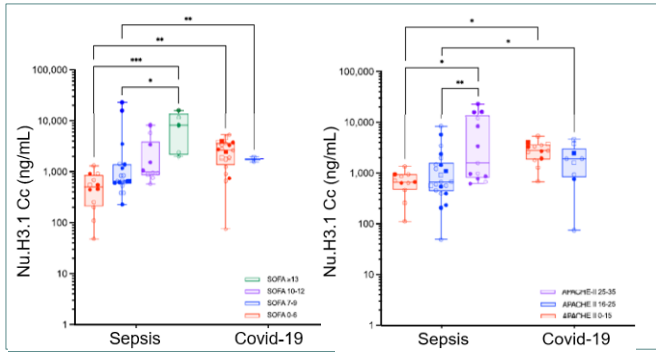
Results

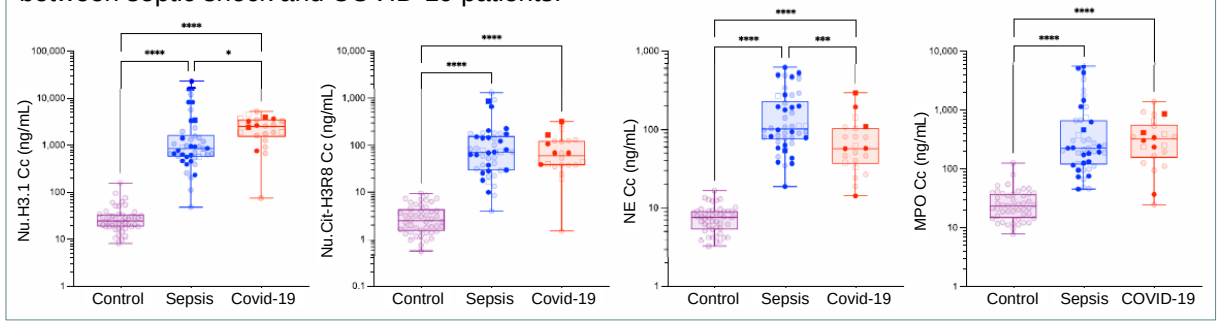


Nu.Q®H3.1 nucleosome levels measured in septic shock patients correlated with SOFA score (adjusted p-value 0.0025) and with APACHE II score (adjusted p-value 0.0321).

No correlation was observed for other biomarkers tested.

Nu.Q®H3.1 levels were higher in COVID-19 and did not correlate with SOFA or APACHE-II scores.

Nu.Q®H3.1, Nu.Q® Cit-H3R8, NE and MPO were compared. All markers were statistically different in septic shock and critical COVID-19 compared to controls. Only Nu.Q®H3.1 and NE were different between septic shock and COVID-19 patients.



Conclusions

- Circulating H3.1- and Cit-H3R8-nucleosomes appear to be interesting markers of global cell death and neutrophil activation.
- H3.1-nucleosomes levels permit the evaluation of disease severity and differ between critical COVID-19 and septic shock patients reflecting two potential distinct pathological processes in these ARDS conditions.
- Further studies are required to confirm nucleosome measurements as predictors of disease severity at an early stage of the disease.