AROTEC News Update: Calprotectin and COVID-19 April 2021

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The dedicated team at AROTEC would like to share the latest publications on the potential use of Calprotectin as a predictive biomarker in COVID-19 patients with its valued customers.

Recent studies have shown that serum Calprotectin is promising biomarker for the early prediction of severe events in critically ill patients with COVID-19. In these studies, serum Calprotectin was deemed superior to traditional acute phase biomarkers such as Procalcitonin (PCT) and C-Reactive Protein (CRP) for the prognosis of the disease. Key references are listed below:

Shi H *et al*. (2020) *Neutrophil calprotectin identifies severe pulmonary disease in COVID-19*. J Leukoc Biol; 1–6. https://doi.org/10.1002/JLB.3COVCRA0720-359R

- The authors measured levels of the neutrophil activation marker Calprotectin in hospitalized patients and determined its relationship to severity of illness and respiratory status.
- Patients with COVID-19 (n = 172) had markedly elevated levels of calprotectin in their blood (in 119 of the 172 patients sampled compared with plasma samples from 50 healthy controls).
- Calprotectin tracked with other acute phase reactants including C-reactive protein, ferritin, lactate dehydrogenase, and absolute neutrophil count, but was superior in identifying patients requiring *mechanical ventilation*.
- The authors concluded that ***Calprotectin was a predictive biomarker of COVID-19 patients likely to progress to respiratory failure*** and who therefore require immunomodulatory treatment.

Silvin A. *et al.* (2020) Elevated Calprotectin and Abnormal Myeloid Cell Subsets Discriminate Severe from Mild COVID-19. Cell. 182, 1401-1418. https://doi.org/10.1016/j.cell.2020.08.002

- This non-interventional study enrolled 158 patients referred to the hospital with various flu-like symptoms. Of these 86 were diagnosed positive and 72 were diagnosed negative with COVID-19 based on RT-PCR of pharyngeal swabs.
- Patients were stratified according to disease severity: Mild disease (n = 27), Moderate disease (n= 16) and Severe disease (n = 43).
- Blood myeloid cells are known to be dysregulated in COVID-19. The authors performed high-dimensional flow cytometry and single-cell RNA sequencing of COVID-19 patient peripheral blood cells and detected disappearance of non-classical $CD14^{Low}CD16^{High}$ monocytes, accumulation of $HLA\text{-}DR^{Low}$ classical monocytes, and release of massive amounts of Calprotectin in severe cases.
- The authors showed the ***Calprotectin level positively correlates with neutrophil count and disease severity such that elevated Calprotectin discriminates severe from mild COVID-19***.

Bauer W. *et al.* (2021) Outcome prediction by serum calprotectin in patients with COVID-19 in the emergency department. J. Infect. 82(4): 84–123. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7670934/

- The authors prospectively enrolled a total of 66 patients presenting to the ED (Emergency Department) with suspected SARS-CoV-2 infection and isolated serum samples for further investigation. Of these 47 patients tested negative and 19 patients tested positive for SARS-CoV-2 and diagnosed with COVID-19 using PCR testing of pharyngeal swabs.
- The disease course was evaluated with regard to the clinical endpoints i) MOF (multi-organ failure) within either 72 h after admission or ii) during the total hospital stay (total MOF), iii) admission to the ICU (Intensive Care Unit), and iv) death, defined as 90-day mortality.
- The authors concluded that that **Calprotectin represents a novel and useful discriminator in COVID-19 patients admitted to the ED with respect to disease outcome, in particular MOF**. In addition, both CRP and PCT may be of low informative value with regard to early patient management in COVID-19 patients evaluated in the ED.

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Guadiana Romualdo, L.G. *et al.* (2021) Circulating levels of GDF-15 and calprotectin for prediction of in-hospital mortality in COVID-19 patients: A case series. J Infect. 82(2): e40–e42.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7419246/

- The authors showed that circulating levels of two emerging inflammatory biomarkers, ***Calprotectin*** and GDF-15, are ***significantly higher in COVID-19 patients who died, suggesting a potential role in the evaluation of prognosis in these patients***.

Udeh R. *et al.* (2021) Calprotectin, an Emerging Biomarker of Interest in COVID-19: A Systematic Review and Meta-Analysis. J. Clin. Med. 10, 775. https://doi.org/10.3390/jcm10040775

- In this study, the authors searched MEDLINE, EMBASE, The Cochrane Library, Web of science & MedRxiv.
- Meta-analysis was done to compare the serum/fecal levels of calprotectin between severe and non-severe COVID-19 infections.
- A total of 10 studies were included in the review (8 had quantitative data while 2 were qualitative). A pooled analysis was conducted of the 8 studies from 613 patients who were RT-PCR positive for COVID-19.
- The authors concluded with high confidence that ***Calprotectin is a foremost candidate biomarker for COVID-19 infections with both diagnostic and prognostic significance***.

Mahler M *et al*. Circulating Calprotectin as a Biomarker of COVID-19 Severity. Expert Review of Clinical Immunology 2021. https://doi.org/10.1080/1744666X.2021.1905526

- The authors searched Pubmed using keywords related to Calprotectin between May 2020 - 8 March 2021.
- **Expert opinion: Calprotectin represents a promising serological biomarker for the risk assessment of COVID-19 patients.**

Whether you already use Calprotectin or have plans to develop an IVD test based on Calprotectin AROTEC will be happy to work with you: we have the products in our portfolio and we have the people and mindset to collaborate with you to make your projects come to fruition. If you'd like to discuss these findings with your AROTEC representative feel free to contact us.

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Product Name/Antigen	Code	Type	Quantity	Source
Calprotectin	ATC04-02	Antigen	0.20 mg	Human Neutrophils
Calprotectin	ATC04-10	Antigen	1.0 mg	Human Neutrophils
Product Name/Antibody	**Code**	**Type**	**Quantity**	**Source**
Anti-Calprotectin Polyclonal	ABC04-10	Antibody	1.0mg	Goat
Anti-Calprotectin Monoclonal	AMC04-02	Antibody	0.20mg	Mouse
Anti-Calprotectin Monoclonal	AMC04-10	Antibody	1.0mg	Mouse

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