Correspondence

European Journal of Emergency Medicine 2022, **29**:315–318

Procalcitonin is a biomarker for disease severity rather than bacterial co-infection in COVID-19

Randeep S. Heer[a], **Amit K.J. Mandal**[a], **Piotr Szawarski**[a] and **Constantinos G. Missouris**[a,b], [a]Department of Medicine, Wexham Park Hospital, Frimley Health NHS Foundation Trust, Slough, UK and [b]Department of Clinical Cardiology, University of Nicosia Medical School, Nicosia, Cyprus

Correspondence to Constantinos G. Missouris, FRCP, FACP, Wexham Park Hospital, Frimley Health NHS Foundation Trust, Wexham Street, Slough, SL2 4HL, UK
Tel: +44 300 614 5000; e-mail: dinos.missouris@nhs.net

Received 2 September 2021 **Accepted** 6 September 2021

Management of patients with severe coronavirus disease 2019 (COVID-19) often includes the use of antibiotics to treat possible secondary bacterial infections. However, identifying those patients with genuine bacterial co-infection remains challenging and the resultant over-prescription of antibiotics has negative implications in terms of antimicrobial resistance and adverse side effects [1]. This has brought about the search for a biomarker to identify COVID-19 patients with true bacterial co-infection. Procalcitonin is a peptide precursor for the hormone calcitonin which is classically used as a diagnostic marker in bacterial infection, however, there is currently insufficient evidence to support its utility as a marker of bacterial co-infection in COVID-19 [2].

We read with interest the work by Malinverni *et al*. who concluded that procalcitonin concentrations measured on admission were unable to differentiate between bacterial and viral pneumonia in COVID-19 patients [3]. Our recently published study evaluated the association between procalcitonin and COVID-19 severity in a critical care setting and whether bacterial co-infection was implicated [4]. We defined bacterial co-infection as positive results from a range of bacterial cultures such as blood, sputum, bronchial lavage, urine and line cultures. Urinary pneumococcal and legionella antigen tests were also included. In contrast to the study by Malinverni *et al*., our study captured the peak procalcitonin concentration measured throughout the critical care admission. There was no statistically significant difference in peak procalcitonin concentrations between patients with positive bacterial cultures compared to those without. Instead, elevated procalcitonin concentrations were associated with inpatient mortality [odds ratio (OR): 2.6; 95% confidence interval (CI), 1.1–6.6, $P = 0.03$) and respiratory failure needing invasive mechanical ventilation (OR: 3.2; 95% CI, 1.3–9.0, $P = 0.02$).

Our findings, like those of Malinverni and colleagues, do not support the role of procalcitonin in identification of bacterial co-infection within the context of COVID-19. Traditionally, it is thought that procalcitonin concentrations remain suppressed in viral infections due to the action of interferon-γ and raised in bacterial infection through increased concentrations of tumor necrosis factor-alpha and interleukin 6 [5]. However, in the absence of proven bacterial co-infection, elevated procalcitonin expression appears to be intrinsically reflective of COVID-19 disease severity through an unelucidated mechanism. We, therefore, propose that procalcitonin should be utilized as a surrogate marker for risk stratification in patients with COVID-19 rather than an indicator of added bacterial infection.

Acknowledgements

All authors contributed to the article and were involved in its final approval.

C.G.M. is acting as a guarantor of the submitted work.

This study was approved by our institution's Research, Quality Improvement and Audit Department. This work does not fall under the remit of the National Health Service Research Ethics Committees. It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Conflicts of interest

There are no conflicts of interest.

References

1 Langford BJ, So M, Raybardhan S, Leung V, Soucy JR, Westwood D, *et al*. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. *Clin Microbiol Infect* 2021; **27**:520–531.
2 Vazzana N, Dipaola F, Ognibene S. Procalcitonin and secondary bacterial infections in COVID-19: association with disease severity and outcomes. *Acta Clin Belg* 2020. doi: 10.1080/17843286.2020.1824749 [Epub ahead of print]
3 Malinverni S, Nuñez M, Cotton F, Martiny D, Collot V, Konopnicki D, *et al*. Is procalcitonin a reliable marker of bacterial community-acquired pneumonia in adults admitted to the emergency department during SARS-CoV-2 pandemic? *Eur J Emerg Med* 2021; **28**:312–314.
4 Heer RS, Mandal AKJ, Kho J, Szawarski P, Csabi P, Grenshaw D, *et al*. Elevated procalcitonin concentrations in severe COVID-19 may not reflect bacterial co-infection. *Ann Clin Biochem* 2021; **58**:520–527.
5 Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. *BMC Med* 2011; **9**:107.

DOI: 10.1097/MEJ.0000000000000882