Clinica Chimica Acta 505 (2020) 190–191

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Letter to the editor

Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis

ARTICLE INFO

Keywords:
Coronavirus
COVID-19
Procalcitonin
Prognosis

Coronavirus disease 2019 (COVID-19), a new form of respiratory and systemic disorder sustained by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is now producing an outbreak of pandemic proportions, whereby nearly 110,000 people have already been infected around the world, 10–15% of whom with severe disease and over 3800 already died [1]. A severe form of pneumonia, potentially evolving towards adult respiratory distress syndrome (ARDS) and occasionally associated with multiorgan failure, are the leading complications of this respiratory virus [2]. Since laboratory medicine provides an essential contribution to the clinical decision making in this and many other infectious diseases [3], we aim to investigate here whether procalcitonin, whose values are not substantially modified in patients with viral infections [4], may play a role in distinguishing patients with or without severe COVID-19.

We carried out an electronic search in Medline (PubMed interface), Scopus and Web of Science, using the keywords “procalcitonin” AND “2019 novel coronavirus” OR “2019-nCoV” OR “COVID-19” without date (i.e., up to March 3, 2020) and language restrictions. The title, abstract and full text of all documents identified according to these search criteria were scrutinized by the authors, and those reporting data in COVID-19 patients with or without severe disease (defined as needing admission to intensive care unit or use of mechanical ventilation), were finally included in our meta-analysis. The reference list of each article was reviewed (forward and backward citation tracking) for identifying other potentially eligible documents. A meta-analysis was then carried out for calculating the individual and pooled odds ratios (OR) with their relative 95% confidence interval (95% CI), using MetaXL software Version 5.3 (EpiGear International Pty Ltd., Sunrise Beach, Australia). Procalcitonin values were entered as dichotomous variable, i.e., below or above the locally defined reference range (typically $\geq$ 0.50 ng/mL). Since the heterogeneity (I^2 statistics) did not exceed 50%, a fixed effects model was finally used.

Overall, 27 articles could be originally identified using our search criteria, 24 of which were excluded after title, abstract or full text reading, because they did not report procalcitonin values in patients with or without severe COVID-19. An additional document could be identified from the reference list of one of selected articles. Overall, 4 studies were finally included in our meta-analysis [5–8]. The pooled OR of these studies is summarized in Fig. 1, which shows that increased procalcitonin values are associated with a nearly 5-fold higher risk of severe SARS-CoV-2 infection (OR, 4.76; 95% CI, 2.74–8.29). The heterogeneity among the different studies was found to be modest (i.e., 34%) [9].

Although the overall number of COVID-19 patients with increased procalcitonin values seems limited, as highlighted in a recent article [10], the results of this concise meta-analysis of the literature would suggest that serial procalcitonin measurement may play a role for predicting evolution towards a more severe form of disease. There is a plausible explanation for this evidence. The production and release into the circulation of procalcitonin from extrathyroidal sources is enormously amplified during bacterial infections, actively sustained by enhanced concentrations of interleukin (IL)-1β, tumor necrosis factor (TNF)-α and IL-6. Nevertheless, the synthesis of this biomarker is inhibited by interferon (INF)-γ, whose concentration increases during viral infections. It is hence not surprising that the procalcitonin value would remain within the reference range in several patients with non-complicated SARS-CoV-2 infection, whereby its substantial increase would reflect bacterial coinfection in those developing severe form of disease, thus contributing to complicate the clinical picture, as recently shown in children with viral lower respiratory tract infections [11]. Additional studies are compellingly needed to verify the putative bacterial origin of procalcitonin increase in patients with severe COVID-19.

https://doi.org/10.1016/j.cca.2020.03.004
Received 3 March 2020; Accepted 3 March 2020
Available online 04 March 2020
0009-8981/ © 2020 Elsevier B.V. All rights reserved.

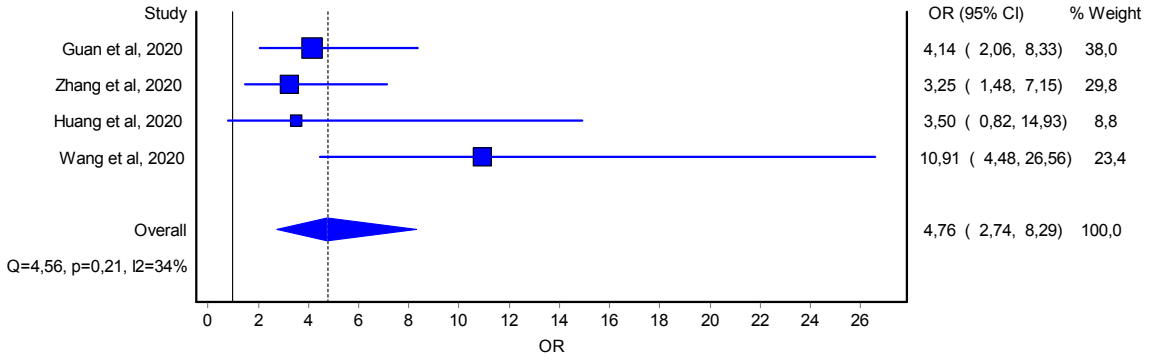

Fig. 1. Odds ratio (OR) and 95% confidence interval (95% CI) of procalcitonin values above the normal reference range for predicting severe coronavirus disease 2019 (COVID-19).

References

[1] World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 49. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/. Last accessed, March 9, 2020.

[2] C. Mattiuzzi, G. Lippi, Which lessons shall we learn from the 2019 novel coronavirus outbreak? Ann. Transl. Med. 8 (2020) 48.

[3] G. Cervellin, P. Schuetz, G. Lippi, Toward a holistic approach for diagnosing sepsis in the emergency department, Adv. Clin. Chem. 92 (2019) 201–216.

[4] P. Schuetz, W. Albrich, B. Mueller, Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future, BMC Med. 9 (2011) 107.

[5] Wei-jie Guan, Zheng-yi Ni, Yu Hu, Wen-hua Liang, Chun-quan Ou, Jian-xing He, Lei Liu, Hong Shan, Chun-liang Lei, David S.C. Hui, Bin Du, Lan-juan Li, Guang Zeng, Kwok-Yung Yuen, Ru-chong Chen, Chun-li Tang, Tao Wang, Ping-yan Chen, Jie Xiang, Shi-yue Li, Jin-lin Wang, Zi-jing Liang, Yi-xiang Peng, Li Wei, Yong Liu, Ya-hua Hu, Peng Peng, Jian-ming Wang, Ji-yang Liu, Zhong Chen, Gang Li, Zhi-jian Zheng, Shao-qin Qiu, Jie Luo, Chang-jiang Ye, Shao-yong Zhu, Nan-shan Zhong, Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. (2020), https://doi.org/10.1056/NEJMoa2002032.

[6] J.J. Zhang, X. Dong, Y.Y. Cao, Y.D. Yuan, Y.B. Yang, Y.Q. Yan, et al., Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China, Allergy (2020), https://doi.org/10.1111/all.14238 (Epub ahead of print).

[7] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Lancet 395 (2020) 497–506.

[8] Dawei Wang, Bo Hu, Chang Hu, Fangfang Zhu, Xing Liu, Jing Zhang, Binbin Wang, Hui Xiang, Zhenshun Cheng, Yong Xiong, Yan Zhao, Yirong Li, Xinghuan Wang, Zhiyong Peng, Clinical Characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China, JAMA (2020), https://doi.org/10.1001/jama.2020.1585.

[9] J.P. Higgins, S.G. Thompson, J.J. Deeks, D.G. Altman, Measuring inconsistency in meta-analyses, BMJ 327 (2003) 557–560.

[10] Giuseppe Lippi, Mario Plebani, Laboratory abnormalities in patients with COVID-2019 infection, Clin. Chem. Lab. Med. (2020), https://doi.org/10.1515/cclm-2020-0198.

[11] J.J. Kotula 3rd, W.S. Moore 2nd, A. Chopra, J.J. Cies, Association of procalcitonin value and bacterial coinfections in pediatric patients with viral lower respiratory tract infections admitted to the pediatric intensive care unit, J. Pediatr. Pharmacol. Ther. 23 (2018) 466–472.

Giuseppe Lippi[a], Mario Plebani[b,*]

[a] *Section of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy*

[b] *Department of Laboratory Medicine, University Hospital of Padova, Padova, Italy*

E-mail address: mario.plebani@unipd.it (M. Plebani).

* Corresponding author at: Department of Laboratory Medicine, University-Hospital of Padova, Via Giustiniani 2, Padova 35128, Italy.