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IM - COMMENTARY

Procalcitonin in daily clinical practice: an evergreen tool also during a pandemic

Alessandro Russo[1] · Mario Venditti[1] · Giancarlo Ceccarelli[1] · Claudio Maria Mastroianni[1] · Gabriella d'Ettorre[1]

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Procalcitonin (PCT) is widely considered an essential tool for identification and monitoring of patients with suspected and proved bacterial infections, to determine clinical severity and to assess the response to antibiotic therapy [1]. Moreover, recent studies demonstrated the association between PCT values and etiology of infection, with higher PCT concentrations detected in Gram-negative etiology, compared to Gram-positive and fungal infections [2, 3].

In a recent real-world study on hospitalized patients admitted with respiratory symptoms and suspected lower respiratory tract infection (LRTI), Johnson et al. evaluated clinical outcomes and costs associated with PCT use in different clinical situations: patients with pneumonia, heart failure, viral respiratory infection, and chronic obstructive pulmonary disease [4]. Of importance, the PCT assessment was associated with reduced antibiotic use, length of stay, and mortality. Furthermore, patients who underwent PCT testing with a negative result were observed to have a 1.7-day shorter mean duration of antibiotics, a shorter mean length of stay of 1.5 days, and the lowest healthcare costs without an increase in adverse outcomes. Of interest, patients with PCT assessment, regardless of the PCT result, were less likely to be readmitted within 30 days.

As a matter of fact, it is plausible that the PCT concentrations can drive physicians to an early diagnosis and an appropriate choice of therapy, also avoiding readmissions for patients who may have received an incorrect empiric therapy. In the study of Johnson and coworkers, PCT testing results a valid tool to manage not only patients with bacterial LRTI but also those with other etiologies including non-infective and viral causes of hospitalization.

✉ Alessandro Russo
alessandro.russo1982@gmail.com

[1] Department of Public Health and Infectious Diseases, Policlinico "Umberto I", "Sapienza" University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy

To date, PCT can be considered a useful tool for clinicians to manage at time of hospitalization patients with suspected infection by SARS-CoV-2 and to promptly distinguish this population from patients with bacterial etiology (see Fig. 1) [5]. Moreover, PCT results as one of the most important determinant to early detect and to monitor bacterial coinfections and superinfections in COVID-19 patients [5, 6]. Of importance, in a recent experience on 1461 patients with COVID-19, a PCT value > 0.5 ng/mL increased the risk of in-hospital mortality [7]. Finally, in a meta-analysis about risk factors for severity and death during COVID-19, a PCT value > 0.5 ng/mL was associated with a higher risk of progression to critical illness [8].

In vitro and in vivo models showed that PCT synthesis is stimulated by IL-6 and TNFα increase [9]. The inflammatory responses induced in immune cells (but also epithelial and endothelial cells) were demonstrated to be crucial in stimulating a cytokine storm, leading to severe injury also in COVID-19 patients [10]. IL-6 is considered to be one of the key mediator of this cytokine storm, causing lung injury and the progression of COVID-19. As reported in several studies, the levels of serum IL-6 were elevated and IL-6 receptors were significantly expressed in patients affected by SARS-CoV-2 infection [11, 12]. Thus, high PCT values may be associated with severity of SARS-CoV-2 infection and the measurement of PCT, especially in the first days of hospitalization, may help physicians to assess the hyper inflammatory activity and to rule out bacterial and fungal coinfection or superinfection [13, 14].

However, research is needed to clarify if the increase in serum inflammatory markers is directly caused by SARS-CoV-2 or should be considered an indirect consequence of patients' clinical status, especially in a population with chronic diseases that, like infectious diseases, can trigger a chronic proinflammatory state. Patients with such comorbidities are more likely to develop severe COVID-19 than healthy patients, at least partly for a dysfunction of innate immune response, increasing the risk of COVID-19

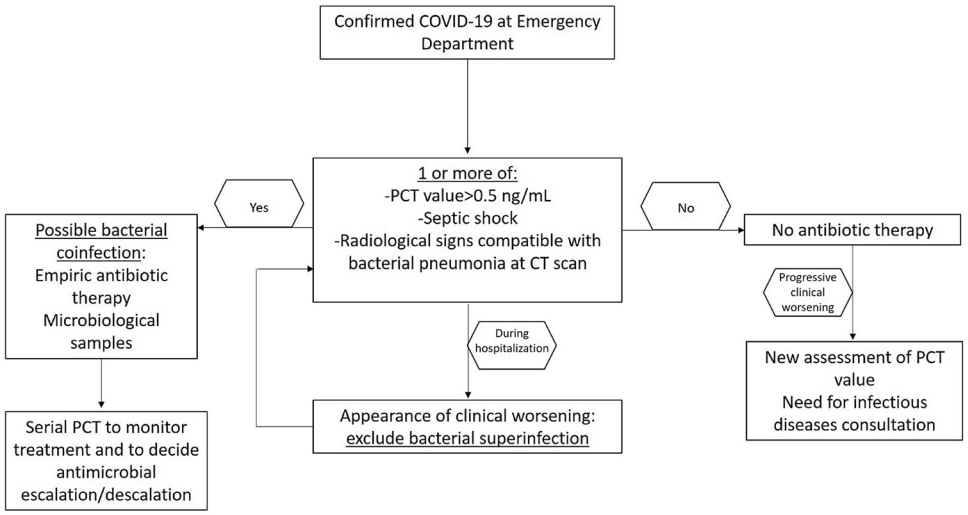

Fig. 1 Management of COVID-19 patients at emergency department and during hospitalization

progression. Monitoring inflammatory markers may represent as an early warning system for progression to a more severe clinical condition.

It is important to underline that monitoring PCT levels can allow early detection of bacterial infections, which may reduce inappropriate prescription of antibiotics or trigger an early antibiotic therapy to treat the first stage of sepsis and other severe infective conditions [15]. Of importance, all the observed advantages associated with PCT utilization in the study of Johnson et al. were limited to patients not requiring intensive care unit (ICU) admission [4]. In this context, the use of PCT resulted to be more efficacious in ICU patients where the decrease of PCT of > 80% over 72 h from ICU admission may provide prognostic information in critically ill patients and drive physicians to the discontinuation of antibiotic therapy [16–18].

In conclusion, the high PCT values reported in COVID-19 patients could be associated with the severity of infection and not only with the presence of bacterial coinfection or superinfection; for all these reasons, the combination of patient's clinical status with laboratory tests and imaging is crucial in daily practice to assess the likelihood of bacterial coinfection in patients with COVID-19 [19], (see Fig. 1). PCT should be included in a diagnostic stewardship to apply the well-known strategies for an appropriate antimicrobial prescription [20].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animal rights Not applicable.

Informed consent Not applicable.

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