Research letter

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Is procalcitonin a reliable marker of bacterial community-acquired pneumonia in adults admitted to the emergency department during SARS-CoV-2 pandemic?

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Clinical manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are disparate and range from common symptoms such as fever, cough, and dyspnoea to less frequent symptoms such as asthenia and fatigue [1]; these symptoms are unspecific and are also found in pneumonia caused by other viruses or bacteria. Severe illness with organ failure, most frequently characterised by an acute respiratory distress syndrome, is observed in approximately 10% of patients; within this group, antibiotics are prescribed for >80% of cases [2]. Differentiating between viral and bacterial pneumonia can be challenging owing to overlap in clinical manifestations [3]. Studies have shown that procalcitonin could be a useful biomarker for clinicians while deciding the antibiotic coverage for patients with community-acquired pneumonia (CAP), as higher serum procalcitonin levels correlate to higher chances of bacterial infections [4] but its usefulness in the COVID-19 pandemic context is unknown. We, therefore, aimed to evaluate the accuracy of procalcitonin to discriminate bacterial from viral CAP in patients infected with SARS-CoV-2.

This retrospective single-centre case–control study included a sample of consecutive patients who visited the emergency department (ED) of CHU Saint-Pierre, Belgium, between 1 March and 21 April 2020. The diagnostic accuracy of procalcitonin in differentiating bacterial from viral CAP was investigated. The inclusion criteria were a suspicion of CAP on admission and a serum procalcitonin test performed during the ED visit. All enrolled patients had clinical signs of a lower respiratory tract infection (LRTI), including at least one symptom of acute respiratory illness (cough, dyspnoea, sputum production, tachypnoea, and pleuritic chest pain) and at least one finding during auscultation (crackles and rales) or one sign of acute infection (temperature >38°C, chills, altered mental status, leucocyte count >10 000/μL or <4000/μL, oxygen saturation ($SatO_2$) breathing ambient air <94% or a loss of ≥4 $SatO_2$ points following a 1-min walking test. Only patients who underwent both bacteriological and virological testing as well as radiological imaging within 48 h after admission were included. During the study period, 3593 patients visited our ED with complaints possibly related to a SARS-CoV-2 infection and 151 were included in the current analysis after applying the inclusion and exclusion criteria. Median time from symptom onset was 7 days [interquartile range (IQR) 5–10]. Among patients with viral CAP, 112 had SARS-CoV-2-related pneumonia.

Procalcitonin concentrations were measured using Lumipulse G B•R•A•H•M•S procalcitonin immunoreaction cartridges. Bacteriological analysis included at least a culture from a respiratory tract specimen or a blood culture. These two exams were performed, respectively, in 43 and 146 patients. SARS-CoV-2 infection was confirmed using the COVID-19 Ag Respi-Strip followed by a quantitative reverse transcription-PCR test in case of a negative result, performed on a nasopharyngeal swab [5]. These tests were performed respectively in 77 and 141 patients. According to clinical manifestations, additional microbiological tests were performed: 16 patients had a urinary Legionella antigen test, 2 patients had a bronchoalveolar lavage and in 1 patient a pleural tap was obtained. Viral serologies contributed to the diagnosis of three patients. In six patients, upon request, respiratory tract specimens were further analysed using multiplex PCR tests, detecting an additional 14 viral and 3 bacterial agents (BioFire FilmArray, bioMérieux, Marcy l'Etoile, France).

CAP was defined as a new infiltrate in a chest radiological study in a patient presenting with LRTI signs and symptoms [6]. Patients were classified as having bacterial CAP if the microbiological analysis revealed a pathogenic bacterium and computed tomography (CT) reported a high suspicion of bacterial pneumonia. Patients were classified as having viral CAP if the patient was not classified as having bacterial CAP and had both a respiratory virus documented in the microbiological analysis and CT reporting a high suspicion of viral pneumonia. Cases that could not be classified according to this method were classified by two independent specialists blinded to procalcitonin results. In case of disagreement, a pneumologist would provide a definitive classification.

Table 1 Cutoff levels, sensitivity and specificity for procalcitonin in detecting bacterial pneumonia

				Patients, no. (%)				PPV	NPV
Value	Cutoff level ng/mL	Sensitivity, % (95% CI)	Specificity, % (95% CI)	True-positive	False-negative	False-positive	True-negative	(95% CI)	
Procalcitonin	>0.1	78.3 (56.3–92.5)	32.0 (24.1–40.9)	18 (11.9)	5 (3.1)	87 (57.6)	41 (27.2)	17.1 (13.9–20.9)	89.1 (78.4–94.9)
(bacterial vs viral	>0.25	60.9 (38.5–80.3)	70.3 (61.6–78.1)	14 (9.2)	9 (6.0)	38 (25.2)	90 (59.6)	26.9 (19.5–36.0)	90.9 (85.6–90.4)
CAP)	>0.5	52.2 (30.6–73.2)	82.0 (74.3–88.3)	12 (8)	11 (7.3)	23 (15.2)	102 (69.5)	34.3 (23.4–47.2)	90.5 (86.1–93.6)

CAP, community-acquired pneumonia; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

We determined the accuracy of procalcitonin to discriminate bacterial from viral CAP by calculating a nonparametric receiver operating characteristic (ROC) curve. The sensitivity, specificity, negative predictive value, and positive predictive value of the procalcitonin test to discriminate bacterial from viral CAP were calculated using procalcitonin cut-offs of 0.1, 0.25, and 0.5 ng/mL (Table 1).

The median procalcitonin level was higher in bacterial (0.53 ng/mL; IQR 0.13–1.56) than viral (0.16 ng/mL; IQR 0.08–0.30) CAP ($P = 0.005$). Using procalcitonin to discriminate between clinically diagnosed bacterial and viral CAP resulted in an area under the ROC curve (AUC) of 0.68 [95% confidence interval (CI), 0.53–0.83). Using a threshold of ≥0.5 ng/mL to identify bacterial CAP resulted in a sensitivity of 52.2% (95% CI, 30.6–73.2%) and a specificity of 82% (95% CI, 74.3–88.2%).

In this monocentric study of 151 adults admitted to the ED during the SARS-CoV-2 pandemic with CAP, including 138 with a microbiologically documented pathogen, no procalcitonin threshold offered accurate discrimination between bacterial and viral CAP as demonstrated by the low AUC of the ROC curve, indicating that procalcitonin had a poor discriminatory power in differentiating bacterial CAP from SARS-CoV-2 associated pneumonia.

While guidelines [6] based on trial results [7,8] discourage the prescription of antibiotics for patients with procalcitonin values ≤0.1 ng/mL and strongly recommend antibiotics for patients with procalcitonin values ≥0.5 ng/mL, results from our study, conducted within the COVID-19 pandemic context, challenge these recommendations. In our cohort, withholding antibiotic treatment in patients with procalcitonin levels ≤0.1 ng/mL would have resulted in not treating 5 (21.7%) of all patients with bacterial CAP. Moreover, the routine administration of antibiotics in patients with procalcitonin ≥0.5 ng/mL would have resulted in inappropriately overtreating 23 (65.7%) of 35 patients with radiological signs of CAP.

The lower discriminatory performance of procalcitonin than that previously reported might be explained by the hyperinflammatory status and the cytokine storm induced by SARS-CoV-2 [9,10] resulting in higher procalcitonin concentrations than those in other viral CAP, thus lowering, in this context, the discriminatory power of procalcitonin for bacterial CAP.

The limitations of our study are its retrospective design, which may have introduced a selection bias; the small sample size; and the monocentric design, which might limit its generalisation.

To conclude, procalcitonin measurements on ED admission during the COVID-19 pandemic cannot accurately differentiate between the bacterial and viral aetiology of CAP.

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The work has not been presented to any meeting so far.

The current study was approved by the Ethical Board of CHU Saint Pierre with the code CE/20-04-18 the 16/04/2020.

The complete dataset of the study will be available in figshare depository at the following URL https://figshare.com/s/2d5d766db8c0c6857ed9 with the following DOI: 10.6084/m9.figshare.12496790.

All authors confirm that they have read and approved the article. All authors to confirm that they have met the criteria for authorship as established by the International Committee of Medical Journal Editors, believe that the article represents honest work, and are able to verify the validity of the results reported. All authors take responsibility for the article as a whole.

Conflicts of interest

There are no conflicts of interest.

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