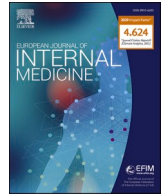




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## Letter to the Editor



## Experience with procalcitonin use during the COVID-19 pandemic

Dear Editor,

Procalcitonin (PCT) is a protein precursor of calcitonin that has been proposed to differentiate systemic inflammation of bacterial origin from viral. The lack of rise in viral infections may be due to virus stimulated production of interferon gamma by macrophages, which inhibits TNF- $\alpha$  in the immune response. Lower PCT levels have a 94% negative predictive value for bacterial co-infection in intensive care unit (ICU) for patients with confirmed influenza A [1].

Although there are few studies showing PCT as a prognostic factor, independent of bacterial infection [2,3], there are many others that demonstrate the use of PCT as an antibiotic stewardship tool leading to a safe reduction in the use of antibiotics in hospitalized non critically ill patients with pneumonia due to coronavirus disease 2019 (COVID-19) [4].

In the United Kingdom, PCT has been used only in ICU until the pandemic. We introduced the use of PCT as a biomarker in the COVID Unit/wards at the Great Western Hospital (GWH) in Swindon for patients with severe COVID-19 pneumonia (defined as SpO<sub>2</sub>  $\leq$  94%) in December 2020, with a clear algorithm that advised to check PCT on admission and at 72 h to allow to safely stop antibiotics if PCT  $<$  0.25.

A meta-analysis of 3 observational studies (169 patients) during 1 week period in the months of December 2020, February and March 2021 was conducted in our hospital to analyse the adherence to the trust protocol on the use of procalcitonin in suspected COVID-19 cases and the reduction of antibiotics as a consequence.

Finally, we conducted a separate study to assess the prognostic value of PCT in patients admitted to ICU with COVID-19 pneumonia ( $n$ : 29 during October 2021).

In our meta-analysis we did record the number of PCT requested, the time of request and the total global antibiotic prescription in patients with severe and non-severe COVID-19 pneumonitis and the number of antibiotics stopped after PCT results.

Our study found that after education and clinical use, the adherence to the protocol improved in GWH during the last year, and the appropriate request of PCT increased from 22% in December 2020 to 76% in October 2021.

The highlight is the significant reduction of global antibiotic prescription from 60 to 70% in December 2020 to 36.5% in October 2021. The antibiotic stop rate after a low procalcitonin ( $<$ 0.25 units) was around 35%.

Although there is still room for improvement, the data shows that procalcitonin has been a successful decision aid tool in affecting clinician attitude to non-bacterial infections such as SARS-CoV-2.

This tool will help to achieve the 10% reduction of annual antibiotic consumption required by the National Health Service trusts (Fig. 1).

In our second study looking at the prognostic value of PCT in patients admitted to ICU, 29 patients were analysed: mean-age was 48.2 years (range 15–74), sex ratio was: M 18/F 10, mean length of ICU stay was: 9.6 (1–37). As per the outcomes, 18 were discharged, 8 died and 2 were transferred.

The results looking at the different groups of patients according to PCT value outcome and antibiotic use were:

PCT  $<$  0.25 ( $n$  = 14): 57% discharged from ICU, 28.5% died, 14.2% transferred to other hospitals. In this group only 2 patients were given antibiotics and 1 was stopped after repeat PCT, (1 not recorded).

PCT: 0.25–0.50 ( $n$  = 8): 87.5% discharged from ICU, 12.5% died. Only 3 patients given antibiotic, 1 stopped after PCT.

PCT  $>$  0.50 ( $n$  = 5): 60% discharged, 40% died. All received antibiotics.

The results of this study do not support the use of this biomarker as an indicator of disease severity for patients with COVID-19 pneumonia admitted to ICU. The majority of patients in this study have a low PCT  $<$  0.25 (58.3%), followed by intermediate value 0.25–0.50 (28.5%) and the high PCT  $>$  0.5 is only present in 17.8%. These results contradict the proposition of previous studies suggesting that higher peak of PCT concentrations correlate with the requirement for invasive mechanical ventilation.

The outcome of these patients has no strong correlation with the PCT value, and although the number of patients surviving ICU is higher in the low/intermediate PCT groups, there are deaths recorded in the low PCT group as well. It is of notice that none of the patients that survived ICU has a repeat PCT  $>$  0.50.

Regarding antibiotics use in ICU in the case of COVID-19 pneumonitis, it is remarkable the good adherence to value of PCT as a guide for prescription.

Our study is small and limited by the fact that other risk factors/comorbidities possibly associated with patients' death are not taken in account. It's clear that PCT alone is not a good prognostic factor of risk for admission to ICU and outcome from the Unit.

PROCALCITONIN PCT in COVID-19 wards	Dec 2020	Feb 2021	Oct 2021
Total patients analysed	62	44	63
Severe COVID-19 pneumonia	45 (72.6%)	26 (59.1%)	25 (39.7%)
PCT requested when indicated:severe COVID-19	10/45 :22.2%	18/26: 69.2%	19/25: 76%
No of PCT level Within range	<0.25: 6/10,60% 0.25-50: 1/10,10% >0.50: 3/10,30%	<0.25: 12/18, 66.7% 0.25-0.50: 2/18, 11.1% >0.50: 4/18, 22.2%	<0.25: 16/19, 84.2% 0.25-0.50: 3/19, 15.7% >0.50: 0/19
Global antibiotics prescribed for patients with COVID-19	71%	61.4%	36.5%
Antibiotics stopped after results of PCT	40%	44%	26.3%

Fig. 1. Meta-analysis of PCT in patients with COVID-19/antibiotics use.

### Declaration of Competing Interest

Nothing to declare

### References

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