Letter to the Editor

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Letter in reply to the letter to the editor of Harte JV and Mykytiv V with the title "A panhaemocytometric approach to COVID-19: a retrospective study on the importance of monocyte and neutrophil population data"

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To the Editor,

We thank Harte and Mykytiv [1] for their interest in our study [2]. In a retrospective cohort of suspected COVID-19 patients, they provide further support for our finding that functional alterations indicative of activation of immunocompetent cells as well as depression of myeloid and lymphoid lineages can be observed in COVID-19 with routine haematology analysers. Such replication in a population of reasonable size is relevant in view of the rush of papers on COVID-19 and the risk of spurious results [3] associated with the earlier, often smaller studies on cell population data (CPD) in COVID-19.

In addition, Harte and Mykytiv, further discuss the role of activated monocytes and neutrophils in COVID-19. In this regard, Wilk et al. [4] identified a reconfiguration of the peripheral immune competent cells. Using a single cell RNA sequencing approach, they demonstrated a continuum of cellular phenotype between developing neutrophils and plasmablasts. This continuum was especially noticed in patients with acute respiratory distress syndrome (ARDS). This new information on phenotypical changes in COVID-19 patients must be kept in mind when interpreting the CPD data of the panhaemocytometric analysis, especially in the follow-up of patients.

Further, Chevrier et al. [5] showed in their recent study a stronger inflammatory phenotype of the neutrophils and monocytes throughout the disease course of patients experiencing severe COVID-19, and this was even more pronounced at later stages of the disease. The distinct temporal changes in immune signatures of these cell types are also reflected in morphological and structural changes that can easily be objectified by haemocytometric follow-up of these patients.

Notwithstanding the similarities between the results of our study and that of Harte and Mykytiv, Harte and Mykitiv observed a less pronounced difference in neutrophil counts between patients with and without COVID-19. This may be related to differences in the selection of patients (i.e. all patients tested for COVID-19 vs. patients with respiratory symptoms only).

Importantly, Harte and Mykytiv make a case for what they call a panhaemocytometric approach to monitoring of COVID-19. Indeed, recent literature supports considering the entire haematological system and the use CPD of data. For example, CPD data obtained with haemocytometers from Sysmex (Kobe, Japan) [6] and Beckman Coulter (Brea, USA) [7] were applied for the diagnosis of COVID-19. Similarly, a prognostic score that included neutrophil and lymphocyte counts as well as measures of granulocyte maturity, activation status of monocytes and lymphocytes, and erythropoiesis, could predict clinical severity in patients hospitalized for COVID-19 [8].

Future research may identify and validate additional applications of CPD parameters in COVID-19 (e.g., early detection of infectious and non-infectious complications) and other diseases as well. Nevertheless, we reiterate that studies on transferability and harmonisation are warranted to facilitate more widespread clinical use of innovative CPD parameters [9].

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In this regard, the concepts behind the CPD parameters used in the aforementioned studies may be applied to analytical platforms of other manufacturers, which, indeed, already provide related parameters [8]. However, complex challenges related to differences in technologies and commercial interests will need to be overcome to make transferability and harmonisation efforts successful [9].

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Competing interest: Remy Martens and Mathie Leers have nothing to disclose. Two permanent employees of Sysmex helped us with retrieving the raw measurement data from our haematology analysers and converted it into readable CSV-files for our recent study on haemocytometric characteristics in COVID-19 [2].

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Ethical approval: Not applicable.

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