

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

FISEVIER

Contents lists available at ScienceDirect

Microbes and Infection

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



Letter to the editor

Personalized stewardship and interdisciplinarity: key elements of COVID-19



Dear Editor,

It has almost been a year since the outbreak of SARS-CoV-2. As this disease has spread around the world, it has changed our approaches to many aspects of everyday life as well as to medicine and health care, including infection control and the evaluation of hospital bed resources. At the beginning of the pandemic, we compared SARS-CoV-2 pneumonia to previously known respiratory viral infections, but then we realised its uniqueness. Although the initial focus was on lung infection and respiratory care, we quickly began to implement interdisciplinary treatment measures. The scientific community and front-line physicians began to analyse every detail of this novel virus (the devil is, after all, in the details). Diving into the depths of this deceptive disease, we eventually moved from a perspective of antimicrobial stewardship (AS) to an assessment of COVID-19 that uses interdisciplinary stewardship. The dysregulated release of cytokines has been identified as a critical factor in negative outcomes, illustrating the paradigms of inflammation and coagulopathies driven by a viral infection [1]. During this wretched journey, we have been learning from those who stand beside us, including intensive care physicians, pulmonologists, rheumatologists, cardiologists, internists, rehabilitators and, of course, our beloved patients. Indubitably, the typical components of stewardship play a role in treating patients with COVID-19. There is a room to discuss the appropriate use of antibiotics, as well as the use of blood cultures and serological and microbiological tests to diagnose admitted COVID-19 patients and the relatively low diagnostic yield of such tests, especially early in the progression of the disease [2]. Bacterial and fungal co-infections are rare in the first stages of the disease, occurring most often in critically ill patients [2,3], making the use of antibiotics often unnecessary and sometimes self-defeating. Can we rely on the factors used to make decisions about other, more well-known respiratory infections when treating patients with COVID-19? What elements should be used to assess patients? We can learn much from our ongoing experiences with COVID-19, and we must choose the correct path based on our experience so far.

Yang et al. [3] analysed the characteristics of asymptomatic and pre-symptomatic patients infected with SARS-CoV-2. They found that in the early stages, shortly after infection, the computed tomography (CT) scans and blood tests of asymptomatic patients differed to those of pre-symptomatic patients. Normal chest CT scans were observed in 35.4% of asymptomatic patients but only in 3.3% of pre-symptomatic patients (P < 0.001) [3]. Compared to asymptomatic patients, pre-symptomatic COVID-19 patients

presented with significantly worse lymphocyte, albumin, transaminase, γ -glutamyl transpeptidase, globulin, creatinine, lactate dehydrogenase, C-reactive protein and erythrocyte sedimentation counts [3]. Moreover, post-mortem biopsies in COVID-19 subjects [4] indicate that lymphocytic alveolar or interstitial patterns occur during the early stages, later giving way to acute fibrinous organising pneumonia and culminating in diffuse alveolar damage. The different stages of the disease differ clinically, radiologically, biochemically and pathologically. However, the disease often follows a biphasic pattern, with respiratory function worsening between 7 and 10 days after disease onset [1,2].

Personalized stewardship may help optimise the management of admitted COVID-19 patients. However, these guidelines will probably differ from those used before this pandemic, considering the burden on the health care systems. Respiratory and oxygen support are vital treatment strategies for severe COVID-19 infections. Disease course and appropriate timing are critical considerations for the stewardship of COVID-19; the day of illness onset, the need for oxygen support, the risk of superinfection, the severity of pneumonia (calculated using quick scores), and the risk of coagulopathies, adverse events or drug-related toxicity. Therefore, a specific stewardship approach may be proposed based on disease course, calculated with the duration of symptoms (D), the presence of absence of fever (F) and the need for any level of oxygen support (O). Our 'at a glance' stewardship proposal uses a "DFO approach" and a broad, interdisciplinary view of COVID-19 (Fig. 1). "D" stands for the day of illness onset (the number of days since the onset of symptoms); it correlates with the risk of biphasic disease with late respiratory worsening as well as the risk of superinfection, coagulopathy, toxicity. "F" stands for the number of days since the fever has subsided, being a sign of disease improvement and reduced inflammation, not merely of infection. Fever, whether absent, persistent or recurrent, is an essential element to consider in the interdisciplinary management of COVID-19 patients (Fig. 1). "O" refers to the number of days since oxygen support was discontinued. Patients with a DFO of 10-3-4 require different care — whether in hospital or a long-term chronic care facility or only in-home care assistance - than those with a DFO of 7-1-0. In other words, a specific, targeted approach must be quickly designed for each patient based on the clinical situation, the intrinsic characteristics of the patient, the patient's susceptibility to superinfections, and local bacterial epidemiology and specific methods for optimising medical care according to DFO guidelines. Keep an eye on pathogenesis and immuno-infectivethrombotic pathways!

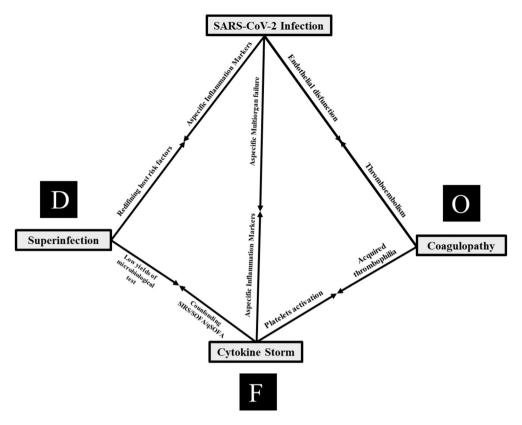


Fig. 1. The pyramid of key elements in COVID-19.

Funding

None.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Declaration of competing interest

None.

Acknowledgements

None.

References

- [1] de la Rica R, Borges M, Gonzalez-Freire M. COVID-19: in the eye of the cytokine storm. Front Immunol 2020 Sep 24;11:558898. https://doi.org/10.3389/ fimmu.2020.558898. PMID: 33072097; PMCID: PMC7541915.
- [2] Rothe K, Feihl S, Schneider J, Wallnöfer F, Wurst M, Lukas M, et al. Rates of bacterial co-infections and antimicrobial use in COVID-19 patients: a retrospective cohort study in light of antibiotic stewardship. Eur J Clin Microbiol Infect Dis 2020 Nov 2:1–11. https://doi.org/10.1007/s10096-020-04063-8. Epub ahead of print. PMID: 33140176; PMCID: PMC7605734.

- [3] Yang R, Gui X, Gao S, Ke H, Xiong Y. Clinical progression and changes of chest CT findings among asymptomatic and pre-symptomatic patients with SARS-CoV-2 infection in Wuhan, China. Expet Rev Respir Med 2020 Nov 2:1–7. https:// doi.org/10.1080/17476348.2021.1840358. Epub ahead of print. PMID: 33135909.
- [4] Copin MC, Parmentier E, Duburcq T, Poissy J, Mathieu D, Lille COVID-19 ICU and Anatomopathology Group. Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection. Intensive Care Med 2020 Jun;46(6):1124-6. https://doi.org/10.1007/s00134-020-06057-8. Epub 2020 Apr 23. PMID: 32328726; PMCID: PMC7178098.

Tommaso Lupia* Department of Medical Sciences, Infectious Diseases, University of Turin, Turin, Italy

Silvia Corcione Department of Medical Sciences, Infectious Diseases, University of Turin, Turin, Italy

Tufts University School of Medicine, Boston, USA

Francesco G. De Rosa Department of Medical Sciences, Infectious Diseases, University of Turin, Turin, Italy

* Corresponding author. Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, Italy. E-mail address: tommaso.lupia89@gmail.com (T. Lupia).

> 11 January 2021 Available online 2 February 2021