



LETTERS TO THE EDITOR

Never Give Up: Lesson learned from a severe COVID-19 patient



To the Editor,

COVID-19 pandemic is causing major health consequences in affected persons needing hospital admission. Since the first epidemic outbreak in China we have learned that several factors including older age, comorbidities and individual immunological responses to infection may differently address the risk of disease progression and outcome.¹ Moreover, there is now quite a unanimous consensus that mortality rate of critically ill patients with SARS-CoV2 pneumonia admitted to Intensive Care Unit (ICU) is really considerable² and even a slightly higher than that recorded in patients with moderate to severe Acute Respiratory Distress Syndrome (ARDS).³

Different attempts using experimental anti-viral⁴ and/or systemic anti-inflammatory drugs^{5,6} have been made to counteract both disease progression and fatal prognosis. Meanwhile, an expert opinion-based document was launched in order to address the early management-related actions for the individual patient, including the choice of an appropriate setting of care and the timing for non-invasive (NIV) or invasive mechanical ventilation (MV).⁷

In light of this, we here report the clinical course of a 72-year old Caucasian male (M.A.) admitted for SARS-CoV2 pneumonia at our University Hospital in Modena on last March 5th. A multidisciplinary medical staff composed of different specialists (infectious diseases, pulmonology,

intensive care) was in charge of care and assuming shared clinical decisions.

Past medical history was characterized by limited atherosclerosis, systemic arterial hypertension, and stable chronic B-cell lymphocytic leukemia (LLC) only requiring periodic follow-up. Onset of symptoms was reported 6 days before admission and infection by SARS-CoV-2 was confirmed by RT-PCR swab nasal/throat samples on the day of admission. Patient presented with fever (38°C), dry cough, tachypnea (respiratory rate-RR=24bpm) and mild respiratory failure (PaO₂/FiO₂ 242 breathing room air). Fig. 1 shows the chest-X-ray and the lung ultrasound pattern on admission (day 1). Given the neurological and hemodynamic stability (Subsequent Organ Failure Assessment-SOFA score was 1) he was admitted to the Infectious Disease Unit where oxygen supply through nasal cannula at the flow of 2L/min and antiviral therapy with darunavir/cobicistat was started in addition to hydroxychloroquine and azithromycin according to our local recommendations. Blood C-reactive Protein (CRP 7.8 mg/dl) was high whereas white blood cell-WBC count (62.510 ml⁻¹) was abnormally increased also due to his LLC condition.

On day 4, patient experienced a major respiratory worsening (PaO₂/FiO₂ 105), with RR > 40bpm) despite oxygen supply at FiO₂ 60%. A multidisciplinary staff evaluation was conducted to balance the need for immediate endotracheal intubation (ETI) and MV with the potential risks derived from his hematological co-morbidity. Decision was taken for a non-ICU care approach thus NIV in pressure support mode was started with the aim to target a pulse oximetry level >90% and a RR <30bpm. At the same time, other anti-

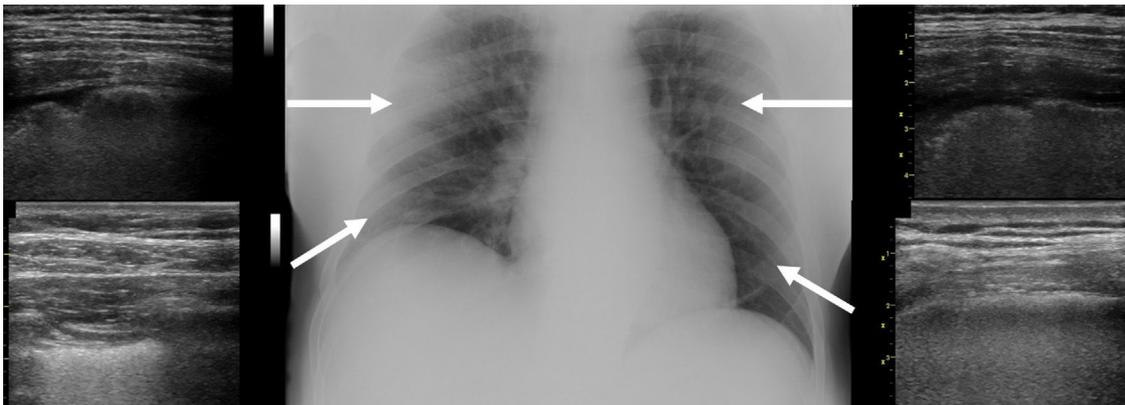


Figure 1 Chest X-ray on admission shows diffuse interstitial abnormalities alongside scattered bilateral infiltrates. Arrows indicate the local ultrasound patterns, in particular: irregular vertical artifacts (B-lines) with impaired pleural sliding next to subpleural small consolidations in the upper anterior sites and thick and confluent B lines in the low posterior site.

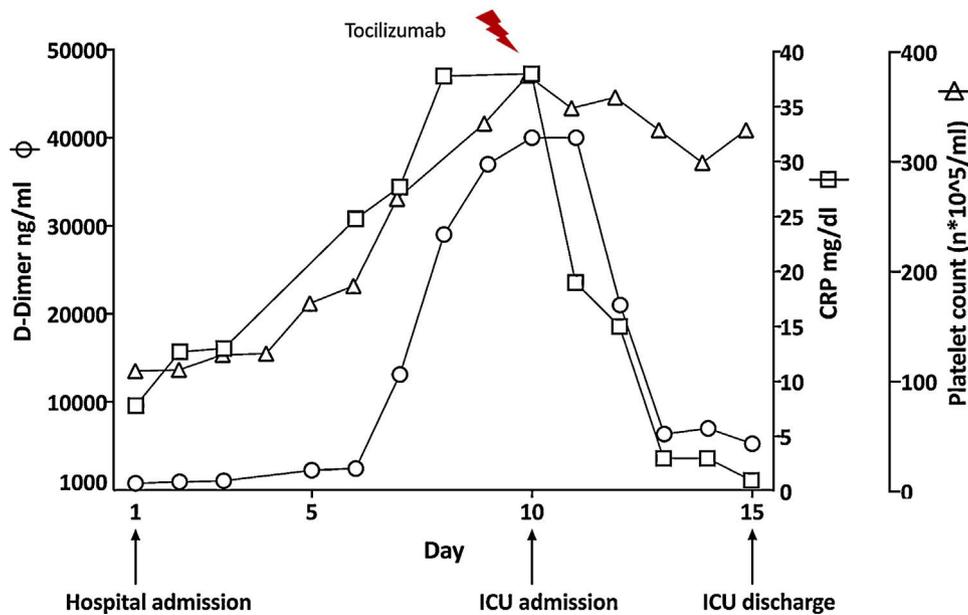


Figure 2 Time course of the inflammatory serum biomarkers D-dimer (circle), CRP (square), and Platelets (triangle), during admission in the COVID-19 area at the University Hospital of Modena.

inflammatory drugs for off-label therapeutic indication were not available in the hospital pharmacy.

From day 5 to 9, patient continued on supported breathing. Finally, he presented uncontrollable respiratory distress despite NIV and maximal oxygen supply ($\text{PaO}_2/\text{FiO}_2 < 100$) on day 10. There was a further multidisciplinary evaluation and, having become available, off-label i.v. Tocilizumab (8 mg/kg of body weight with 2 infusions 12-hour apart)⁶ and admission to ICU for endo-tracheal intubation and mechanical ventilation were adopted as rescue therapies. On day 13 patient's condition and gas exchange improved ($\text{PaO}_2/\text{FiO}_2$ 121) and tracheostomy was performed, while patient progressively returned to an assisted breathing modality. The time course of the main inflammatory serum markers over the admission period is shown in Fig. 2.

On March 18th (day 15), M.A. was transferred to a different hospital in our provincial area (Ospedale di Sassuolo) for weaning purpose. Respiratory condition progressively improved reaching spontaneous breathing on day 23, while a supervised physiotherapy protocol was started due to the consequences of prolonged immobility. Tests to assess the vocal cord and swallow integrity were then performed, according to the recommended procedures, leading on April 6th (day 31) to removal of both the naso-gastric tube and the tracheal cannula. Oxygen supplementation was also withdrawn on the same day. Two consecutive nasal/throat RT-PCR swab samples were confirmed negative for RNA virus and specific immunoglobulin-G were dosed in serum, so patient was discharge as cured and transferred to a rehabilitation unit to complete his recovery (day 33).

The story of M.A. confirms the heavy risk and the long and difficult clinical process behind any severe pneumonia due to SARS-CoV2 infection and prompts several considerations.

First, it is quite clear that the clinical course in patients hospitalized due to pneumonia and worsening respiratory

failure is unforeseeable, thus requiring great attention and prompt action. The complexity, comorbid status and age of the patient only partially explain this variability. Indeed, it has been recently hypothesized that least 3 different grades of increasing severity may be recognized, which correspond to, distinct clinical findings, response to therapy and clinical outcome, and are likely to depend on the balance between the viral phase and the host inflammatory response.⁸

Second, the history of M.A. at least partially proposes the unprecedented decisions to be taken, whether by hospital, physicians and/or nurses, i.e. withhold a ventilator and/or access to ICU when faced with an anticipated shortage of ventilators and ICU-beds during an uncontrolled epidemic outbreak⁹ or with a clinical discussion on a proportionate treatment. This might in turn overexpose clinicians to the risk of civil or criminal liability in the absence of clear Government assurance when facing extraordinary events.¹⁰ Given the particular condition to which M.A. rushed after admission, the decision taken to proportion intensity of respiratory support by NIV could have led to an unwanted liability.

Third, it should be noted that, as tocilizumab was not available to prompt a potentially anti-inflammatory drug effect, even in a later stage as was the case of our patient (see Fig. 2), the choice to use NIV was indeed the only means to "buy time" before any upgraded decision of care could be taken. This highlights the role that noninvasive respiratory support may have during COVID-19 epidemic, which is not only to manage the advanced hypoxic respiratory failure,⁷ but also to help clinicians to assist a very severely ill patient even if at high risk. Ongoing data on this epidemic are showing that the decision to prevent endotracheal intubation by NIV might be a safe option for patients. While we are waiting for more convincing data on the role of anti-inflammatory agents to early brake systemic inflammation and progression of the disease,^{5,11} it has been

discussed whether or not early ETI and MV would be the best option for the COVID-19 patient's outcome.¹² One of the hypotheses behind this is that COVID-19 is not a typical ARDS, so MV in many cases is not the right treatment. COVID-19 patients show significant vasoconstriction of small blood vessels compared to the healthy and ARDS patients. It is known that ventilation reduces the small blood vessel size, meaning it is probably making things worse for most COVID-19 patients. Notably, a very recent audit in UK in over 6000 patients shows that death rate in COVID-19 patients using advanced respiratory support (ETI, MV, ECMO) is significantly higher as compared with patients on basic support (oxygen with inspiratory fraction >50%, CPAP/BIPAP) (66.3 vs. 51.6%, respectively). This in turn expresses a much higher risk rate when compared to that (22%) occurring in a retrospective series of hospitalized non-COVID viral pneumonia.¹³

Finally, present experience has led clinicians to the evidence that such a very severe situation with difficult and risky decisions unavoidably lead the patient to a long clinical course with associated disability.¹⁴ Since beating the virus is just the beginning, any lack of access to early physiotherapy and to a long-term strategy for survivors of severe COVID-19 is a problem to be overcome urgently.¹⁵

From our personal experience during COVID-19 epidemic we encourage colleagues not to give up in all circumstances due to this happily ending story.

(At the time of submission, the smiling photo of M.A. received 1.641 like and 79.712 visualizations on LinkedIn at <https://www.linkedin.com/feed/update/urn:li:activity:6653733697633812481/>)

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Consent to publish data

Informed consent to publish data was obtained from the patient.

Conflicts of interest

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Prevention measures for COVID-19 in retail food stores in Braga, Portugal



COVID-19 is the designation of the World Health Organization for the infectious disease caused by the new coronavirus, which can cause severe respiratory infection, such as pneumonia.¹ The main modes of transmission of COVID-19 are: 1) close contact with people infected by the virus or 2) contact with contaminated surfaces or objects. Transmission takes place through droplets that are expelled when a person with COVID-19 coughs, sneezes or speaks, or through contact with contaminated hands that touch the eyes, nose or mouth of a person (hands are easily contaminated by contact with objects or surfaces where droplets from an infected person have landed).² Knowing that close contacts can contribute to increasing the spread of the infection, breaking these transmission chains is essential.

In this context, the Portuguese Directorate-General of Health (DGS) has been issuing guidelines on the public health measures to be adopted by public service establishments to prevent the spread of the virus.³ Briefly, the best practices recommended by DGS include the following: guarantee that checkout counters maintain physical distance of 1 m; post signage on the floor to help customers maintain adequate social distancing; create physical barriers between employees and customers, in order to avoid “excessive approximation between individuals”. As measures for cleaning and sanitizing, DGS recommends disinfecting the whole store area at least once a day; and frequently cleaning (at all hours) the high-touch surfaces, such as ticket dispenser machines or ATMs. Moreover, alcohol-based solutions should be provided in strategic locations.³ This observational study

aims to describe the measures adopted to prevent the transmission of COVID-19 by retail food stores in the municipality of Braga, Portugal.

To this end, a researcher from the Institute of Education of the University of Minho designed and implemented a descriptive observational study, carried out between 5th and 8th April 2020, with a convenience sample of eight retail food stores in the municipality of Braga (Portugal). Observations and registries were made by three researchers in different types of stores (mini markets, supermarkets, and hypermarkets). Each store was observed once. Researchers were, on average, 10 min in each outlet. Data was collected by filling out a previously prepared form, which included the following variables: I. Measures adopted outside the store (signs of disinfection of the floors; disinfection of shopping carts/baskets; measures to prevent overcrowding; existence of signage that encourages employees and customers to practice health safety procedures such as social distancing and wearing face mask); II. Measures adopted inside the store (indication of the necessary physical distance between people; provision of hand sanitizer, gloves, or other personal protective equipment); III. Employees (cashier: use of a visor or a mask/glasses, use of gloves, existence of acrylic separator walls at counters; store operators: use of a visor or a mask, use of gloves); IV. Customers (gender; age group; use of a surgical or handmade face mask, or a scarf; use of a visor/other; use of gloves).

Six of the eight establishments observed showed signs of disinfection of the floors. Four of them disinfected shopping carts/baskets; almost all employed measures to prevent overcrowding ($n=7$) and all of them displayed signage and warnings about COVID-19. As to measures adopted inside the store, most had indications of the necessary physical