LETTER TO THE EDITOR



Global approaches for global challenges: The possible support of rehabilitation in the management of COVID-19

To the Editor,

We have read with interest the paper by Li et al about the neurotropism of the severe acute respiratory syndrome coronavirus (SARS-CoV-2), responsible of coronavirus disease (COVID-19), recently discovered in China and now worldwide spread. In particular, the paper focuses on the role of the nervous system involvement in causing the respiratory failure. The authors take into consideration the biological similarities of SARS-CoV-2 with two coronaviruses, which globally impacted the recent history: SARS-CoV, discovered in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV), discovered in 2012.^{1,2} Even if the role of neuroinvasion in COVID-19 severity still remains undefined, the authors correctly underline its important implications. In particular, the treatment options should contemplate this potential trait of SARS-CoV-2, for example, considering the obstacle of blood-brain barrier or limiting the use of corticosteroids. The message conveyed by the authors is extremely important and induces specific reflections about COVID-19 management. The lone possibility of the relationship between respiratory failure and neuroinvasion of SARS-CoV-2 should encourage strict clinical monitoring of the patients and research works aimed to clarify the features of this disease.

From a long-term perspective, the alert expressed by Li et al¹ is important for the treatment in postacute phase. In fact, after the clinical stabilization and, hopefully, virus eradication by the use of proper drugs, functional restoration should be the main goal.³ Indeed, the disease can be very severe and its long-term bio-psycho-social consequences potentially very serious.⁴ In this sense, rehabilitation may play a relevant role for the management of postacute COVID-19. This role is not only limited to the design of specific programs, mainly based on physical exercises for respiratory improvement, but should consider a continuous and global control of functions. In addition, the aforementioned neuroinvasive potential of SARS-CoV-2, as expressed in the conclusions of the work by Li et al, 1 represents an insidious danger. This makes the follow-up of patient's functional condition essential and the contribution of rehabilitation determinant. Furthermore, it implies adaptations of specific rehabilitation programs: if the pulmonary damage is associated with neurological impairment, the programs usually developed for pure respiratory diseases could not be enough for patient's recovery.⁵ The rehabilitation approach can be independent of the setting: hospital, intensive care unit (ICU), and home.⁶ Actually,

rehabilitation in ICU, besides the mentioned improvement of the deficits directly determined by the virus-related damages, should prevent secondary impairments, due to immobilization syndrome, and, for example, critical illness of neuropathy and myopathy. This issue is fundamental, especially if associated with the neurotropism of the coronaviruses. Even at home, for patients in compulsory or spontaneous quarantine, rehabilitation management can provide indicative parameters of the multisystem function. By the use of simple self-administrable exams, like Borg scale for perceived exertion or 6-minute-walking test, the subject can check his/her status.⁶ These evaluations can reveal impairments in apparently asymptomatic patients and indicate the necessity of further medical assessments for an early diagnosis. In addition, for convalescent patients at home, rehabilitation programs should be developed for a rapid functional restoration and for a continuous monitoring.³ This tactics should be supported by telerehabilitation systems, based on electronic applications, able to make efficient the communication between patients, caregivers, and healthcare professionals, without the direct contact.⁸ Hence, rehabilitation enlarges its usual field of action, representing a model for secondary and tertiary prevention, and can be a potential aid in the control of COVID-19 diffusion.

To evaluate the impact of rehabilitation in the severe coronavirus diseases, we have started from the analysis by Li et al, who considered SARS-CoV and MERS-CoV. We have searched on PubMed the papers about these viruses, considering a 5-year-period time since the discovery of each virus. Then, we have calculated the percentages of the papers about "nervous system," "rehabilitation," and "neuroinvasive," respect to the total number of papers about a particular virus. The same analysis was performed for the SARS-CoV-2, but just for the time period 2019 to 2020 (Figure 1). Interestingly, the percentage of papers about "nervous system" and "neuroinvasive" is higher in MERS-CoV, in comparison with SARS-CoV. Probably, after the discovery the 2002 coronavirus, the interest about the neurotropism of this kind of viruses increased. Another interesting result is the notable high percentage of papers about "rehabilitation" for SARS-CoV-2. The data, although partial, could support the importance of rehabilitation in the supervision and treatment of acute infections and open the doors for further research works about this topic.

We would like to thank Li et al¹ for their contribution which highlights the complexity of coronavirus diseases and stimulates reflections for the development of healthcare.

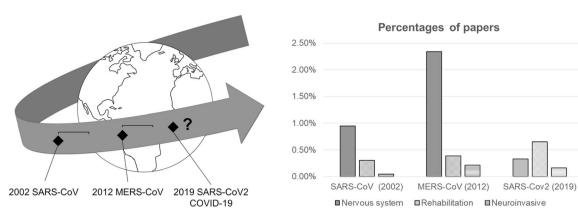


FIGURE 1 In the left panel, a schematic representation of the timeline indicating the year of discovery of the three viruses considered in the paper. The short horizontal lines show the time period considered for the literature review. The question mark indicates the evolving situation of the SARS-CoV-2. In the right panel, the results of the literature research. The colors of the histograms about the SARS-CoV-2 are softer because the results are partial, for the ongoing situation. COVID-2019, coronavirus disease-2019; MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

Daniele Coraci¹ Daniele Coraci¹ Daniele Coraci¹ Augusto Fusco² Antonio Frizziero³ Silvia Giovannini⁴ Lorenzo Biscotti⁴ Luca Padua^{1,5}

¹Neuroriabilitazione ad Alta Intensità, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

²Department of Neurorehabilitation, IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy

³Department of Medicine and Surgery, University of Parma, Parma, Italy ⁴Department of Geriatrics, Neurosciences, and Orthopaedics, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

⁵Department of Geriatrics, Neurosciences and Orthopaedics, Università Cattolica del Sacro Cuore. Rome. Italy

Correspondence

Daniele Coraci, Neuroriabilitazione ad Alta Intensità, Fondazione Policlinico Universitario A. Gemelli IRCCS, 00168 Rome, Italy. Email: danielecoraci@aol.com

ORCID

Daniele Coraci (b) http://orcid.org/0000-0002-7019-9006

REFERENCES

- Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. 2020. https://doi.org/10.1002/jmv.25728
- St-Jean JR, Jacomy H, Desforges M, Vabret A, Freymuth F, Talbot PJ. Human respiratory coronavirus OC43: genetic stability and neuroinvasion. J Virol. 2004;78(16):8824-8834. https://doi.org/10.1128/ JVI.78.16.8824-8834.2004
- 3. Xie L, Liu Y, Xiao Y, et al. Follow-up study on pulmonary function and lung radiographic changes in rehabilitating severe acute respiratory syndrome patients after discharge. *Chest.* 2005;127(6):2119-2124. https://doi.org/10.1378/chest.127.6.2119
- Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. J Med Virol. 2020. https://doi.org/10.1002/jmv.25735
- Wang XL, Ma LJ, Hu XG, Wang K, Cheng JJ. Application of the respiratory "critical care-sub-critical care-rehabilitation integrated management model" in severe stroke associated pneumonia. *BMC Pulm Med*. 2020;20(1):61. https://doi.org/10.1186/s12890-020-1100-7
- Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. Chest. 2007;131(5 Suppl):4S-42S. https://doi.org/10.1378/chest.06-2418
- Bagnato S, Boccagni C, Sant'angelo A, Prestandrea C, Romano MC, Galardi G. Neuromuscular involvement in vegetative and minimally conscious states following acute brain injury. *J Peripher Nerv Syst*. 2011;16(4):315-321. https://doi.org/10.1111/j.1529-8027.2011. 00363.x
- Cox NS, McDonald CF, Alison JA, et al. Telerehabilitation versus traditional centre-based pulmonary rehabilitation for people with chronic respiratory disease: protocol for a randomised controlled trial. BMC Pulm Med. 2018;18(1):71. https://doi.org/10.1186/s12890-018-0646-0