



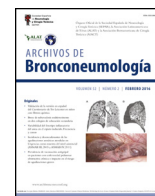
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.



ARCHIVOS DE Bronconeumología

www.archbronconeumol.org



Letter to the Director

Response to Aspirin Therapy in COVID-19: Prevention of NETosis

To the Director,

We thank Kow et al., for the interest in our recently published manuscript “Pre-hospital Aspirin Use and Patient Outcomes in COVID-19”^{1,2} in your esteemed *journal* and for highlighting some interesting points.

The possibility of aspirin having an effect on reducing the neutrophil extracellular trap (NET) is indeed a possibility in the hospitalized COVID-19 patients. Report from Radermecker and team suggested that NETs may have some contribution to distinct traits of COVID-19 physiopathology by infiltrating separate lung compartments. The existence of NETs in the airway compartment could also represent major procoagulant triggers, leading to fibrin deposition and subsequent impaired pulmonary ventilation.³ Several agents have been proposed to interfere with NETs formation through inhibition of TLR9 and to have the therapeutic potential for the COVID-19 disease, but not many of these agents have been proven to show efficacy to reduce the severity of disease progression or other patient centered outcomes.⁴

Kow and team, quite astutely, point out that the RECOVERY trial excluded the patients that were already receiving aspirin therapy as outpatient prior to being admitted in the hospital and therefore the comparison is no longer valid. In addition, there were significant patient characteristic differences between our cohort and the cohort included in the RECOVERY trial. The cohort from the VIRUS registry was older by 10 years with more comorbidities as compared to the cohort in the RECOVERY trial and thereby adding another limitation for a head-to-head comparison of results from these 2 studies.⁵

We agree with the suggestion of conducting future clinical trials investigating the efficacy of aspirin therapy (and potentially other antiplatelet agents as well) in a well-designed experimental fashion. To suggest a practice change for primary/secondary prevention using aspirin for the COVID-19 disease additional rigorous research is needed.

Funding

This publication was supported by NCATS CTSa Grant Number UL1 TR002377. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Authors' Contributions

A.L. and O.G. prepared the main manuscript text and have agreed on final approval of the response letter.

Conflict of Interests

The authors state that they have no conflict of interests.

References

1. Lal A, Garces JPD, Bansal V, Tekin A, Zec S, Khanna AK, et al. Pre-hospital aspirin use and patient outcomes in COVID-19: results from the International Viral Infection and Respiratory Illness Universal Study (VIRUS). *Arch Bronconeumol*. 2022.
2. Lal A, Domecq Garces J, Tekin A, Bansal V, Khanna A, Warner M, et al. Pre-hospital aspirin use and patient outcomes in Covid-19: results from the International Viral Infection and Respiratory Illness Universal Study (Virus). *Arch Bronconeumol*. 2022, p. A2964-A.
3. Radermecker C, Detrembleur N, Guiot J, Cavalier E, Henket M, d'Emal C, et al. Neutrophil extracellular traps infiltrate the lung airway, interstitial, and vascular compartments in severe COVID-19. *J Exp Med*. 2020;217.
4. Pastorek M, Dúbrava M, Celec P. On the origin of neutrophil extracellular traps in COVID-19. *Front Immunol*. 2022;13:821007.
5. Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2022;399:143–51.

Amos Lal*, Ognjen Gajic

Department of Medicine, Division of Pulmonary and Critical Care
Medicine, Mayo Clinic, Rochester, MN, USA

Corresponding author.

E-mail address: Lal.Amos@mayo.edu (A. Lal).

<https://doi.org/10.1016/j.arbres.2022.10.004>

0300-2896/© 2022 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Please cite this article as: A. Lal and O. Gajic, Response to Aspirin Therapy in COVID-19: Prevention of NETosis, *Archivos de Bronconeumología*, <https://doi.org/10.1016/j.arbres.2022.10.004>