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## European Journal of Internal Medicine

journal homepage: [www.elsevier.com/locate/ejim](https://www.elsevier.com/locate/ejim)**Colchicine for the prevention of COVID-19 “hard” outcomes: All that glitters is not gold***Dear Editor,*

In a paper recently published in the European Journal of Internal Medicine, Schattner provided a thorough and in-depth review regarding the multiple, pleiotropic effects of colchicine, also highlighting its potential beneficial effects in coronavirus disease 2019 (COVID-19) [1]. In their commentary, Kow et al. [2] emphasize on the need for further trials with a longer treatment duration for the assessment of colchicine's therapeutic efficacy, dampening the initial enthusiasm. Previous meta-analyses of observational studies and randomized controlled trials demonstrated a mortality benefit with colchicine in patients with COVID-19, leading to the amendment of treatment protocols against the disease worldwide [3,4].

Upon the recent publication of further randomized controlled trials, we sought to determine whether colchicine compared to standard of care offers a true benefit, both in the in-hospital and out of hospital setting, for the prevention of surrogate COVID-19 outcomes. We searched PubMed and Cochrane Library databases for relevant published randomized controlled trials up to 12th November 2021. We set as primary efficacy outcome the surrogate endpoint of COVID-19 death and as secondary efficacy outcome that of mechanical ventilation. We extracted the data from the eligible reports, by using a pilot tested, data extraction form.

As we assessed only dichotomous variables, differences were calculated with the use of risk ratios (RR), with 95% confidence interval (CI), after implementation of the Mantel-Haenszel (M-H) random effects

formula. Statistical heterogeneity among studies was assessed by using  $I^2$  statistics. All analyses were performed at the 0.05 significance level, while they were undertaken with RevMan 5.3 software.

We finally included 6 randomized controlled trials [5–10] in a total of 15,624 subjects with documented COVID-19 infection. All trials except for one [8] enrolled hospitalized patients. As shown in Fig. 1, colchicine was not superior to standard of care in terms of prevention of COVID-19 death (RR = 0.63, 95% CI; 0.33 – 1.20,  $I^2 = 28%$ ). In addition, colchicine did not result in a significant decrease in the risk for mechanical ventilation during disease course (RR = 0.66, 95% CI; 0.36 – 1.20,  $I^2 = 48%$ ), as shown in Fig. 2.

The present pooled analysis of relevant, published randomized controlled trials so far does not support the routine use of colchicine for the prevention of surrogate COVID-19 outcomes in daily clinical practice, either in the in-hospital or in the community therapeutic management of patients with COVID-19. Whether colchicine can positively affect the prognosis of COVID-19 in specific patients' populations, such as those suffering from autoinflammatory diseases [11], has to be further confirmed in randomized controlled trials, besides hypothesis-generating observational studies.

**Funding**

None.

<https://doi.org/10.1016/j.ejim.2021.11.016>

Received 13 November 2021; Accepted 18 November 2021

Available online 25 November 2021

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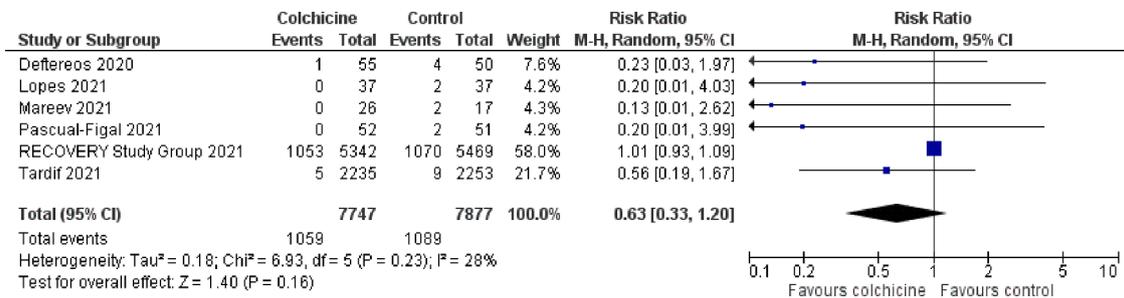


Fig. 1. Effect of colchicine compared to control on the risk for COVID-19 death.

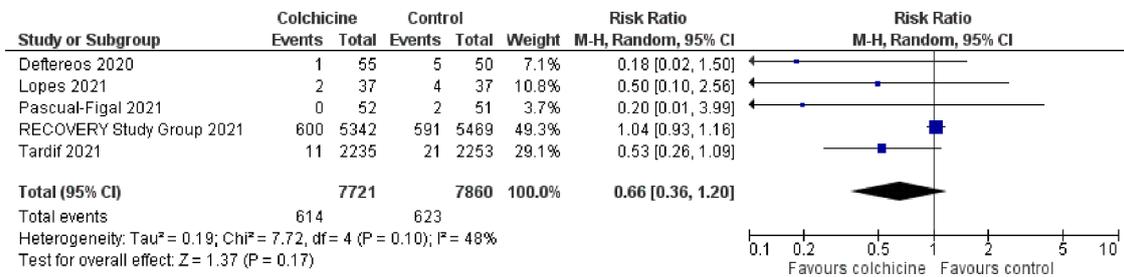


Fig. 2. Effect of colchicine compared to control on the risk for mechanical ventilation due to COVID-19.

## Acknowledgments

None.

## Declaration of Competing Interest

None declared.

## References

- [1] Schattner A. Colchicine-new horizons for an ancient drug. *Eur J Intern Med* 2021. <https://doi.org/10.1016/j.ejim.2021.10.002>.
- [2] Kow Siang C, Sangarran Ramachandram D, Shahzad Hasan S. Colchicine for COVID-19: hype or hope? *Eur J Intern Med* 2021. <https://doi.org/10.1016/j.ejim.2021.11.011>.
- [3] Nawangsih EN, Kusmala YY, Rakhmat II, et al. Colchicine and mortality in patients with coronavirus disease 2019 (COVID-19) pneumonia: a systematic review, meta-analysis, and meta-regression. *Int Immunopharmacol* 2021;96:107723. <https://doi.org/10.1016/j.intimp.2021.107723>.
- [4] Elshafei MN, El-Bardissy A, Khalil A, et al. Colchicine use might be associated with lower mortality in COVID-19 patients: a meta-analysis. *Eur J Clin Invest* 2021;51(9):e13645. <https://doi.org/10.1111/eci.13645>.
- [5] RECOVERY Collaborative Group. Colchicine in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial [published online ahead of print, 2021 Oct 18]. *Lancet Respir Med* 2021. [https://doi.org/10.1016/S2213-2600\(21\)00435-5](https://doi.org/10.1016/S2213-2600(21)00435-5). S2213-2600(21)00435-5.
- [6] Deftereos SG, Giannopoulos G, Vrachatis DA, et al. Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: the GRECCO-19 Randomized Clinical Trial. *JAMA Netw Open* 2020;3(6):e2013136. <https://doi.org/10.1001/jama-networkopen.2020.13136>. Published 2020 Jun 1.
- [7] Lopes MI, Bonjorno LP, Giannini MC, et al. Beneficial effects of colchicine for moderate to severe COVID-19: a randomised, double-blinded, placebo-controlled

clinical trial. *RMD Open* 2021;7(1):e001455. <https://doi.org/10.1136/rmdopen-2020-001455>.

- [8] Tardif JC, Bouabdallaoui N, L'Allier PL, et al. Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. *Lancet Respir Med* 2021;9(8):924–32. [https://doi.org/10.1016/S2213-2600\(21\)00222-8](https://doi.org/10.1016/S2213-2600(21)00222-8).
- [9] Pascual-Figal DA, Roura-Piloto AE, Moral-Escudero E, et al. Colchicine in Recently Hospitalized Patients with COVID-19: a Randomized Controlled Trial (COL-COVID). *Int J Gen Med* 2021;14:5517–26. <https://doi.org/10.2147/IJGM.S329810>. Published 2021 Sep 11.
- [10] Mareev VY, Orlova YA, Plisyk AG, et al. Proactive anti-inflammatory therapy with colchicine in the treatment of advanced stages of new coronavirus infection. The first results of the COLORIT study. *Kardiologiia* 2021;61(2):15–27. <https://doi.org/10.18087/cardio.2021.2.n1560>. Published 2021 Mar 1.
- [11] Nas K, Eryilmaz N, Geyik MF, Altaş A. COVID-19 in patients with familial Mediterranean fever treated with colchicine: case based review. *Rheumatol Int* 2021;41(4):811–7. <https://doi.org/10.1007/s00296-021-04809-3>.

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