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.

time frame analysis showed a significant drop in hospitalization rates just after PC encounters, and continued to decrease over time (*Panel* A). The annual trends for 90-day all-cause hospitalization rates before PC encounters showed a significant reduction over time (59.7% in 2010 to 53.3% in 2018, p <0.001), but hospitalization rates after PC remained stable over the study period (*Panel* B).

In this observational nationwide analysis of over 25,000 acute on chronic HF admissions, PC encounters were associated with a significant reduction in all-cause, HF-specific, and non-HF 90-day hospitalization rates. This reduction was noted immediately after discharge from the index admission with a PC encounter. Hospitalization rates before PC utilization decreased over the study period perhaps due to the early recognition of value of PC among these sick patients.

This study is limited by the nature of this administrative database which carries a risk of mis- or under-coding. Additionally, we could not identify patients who died after hospital discharge. Some of the reduction in readmission may be due to this factor. However, it is unlikely that death would account for the entire decrease in admission rates after a hospital PC consultation, since not all patients seen by PC physicians are appropriate for hospice or accept a palliative approach to care, and the previously reported post-HF discharge 30-day mortality rate ~7% (1). Moreover, the philosophical change of care to a palliative approach encourages a decrease in low-value health care utilization such as repeat hospital admissions at the end of life. In summary, we found that patients who received a PC encounter during a hospitalization had a reduction in subsequent readmission rates. Further studies should assess the competing risk of death in this population.

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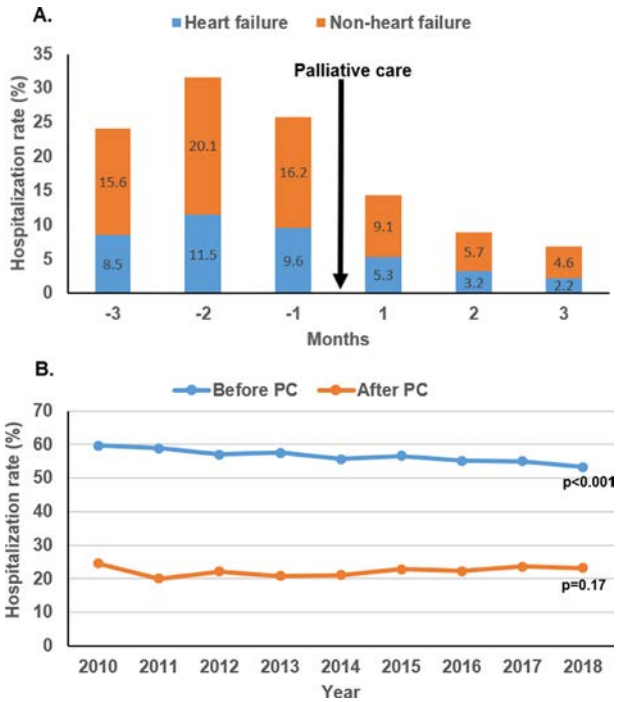

Figure. ***Panel A***, Monthly heart failure and non-heart failure hospitalization rates before and after palliative care encounters. ***Panel B***, Annual trends of all-cause 90-day hospitalization rates before and after palliative care encounters. PC=palliative care.

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1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Shay CM, Spartano NL, Stokes A, Tirschwell DL, VanWagner LB, Tsao CW, American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation* 2020;141:e139–e596.
2. Diop MS, Bowen GS, Jiang L, Wu WC, Cornell PY, Gozalo P, Rudolph JL. Palliative care consultation reduces heart failure transitions: a matched analysis. *J Am Heart Assoc* 2020;9:e013989.
3. Overview of the Nationwide Readmissions Database. Healthcare Cost and Utilization Project. https://www.hcup-us.ahrq.gov/nrdoverview.jsp. Accessed January 5, 2021.
4. Elgendy IY, Elbadawi A, Sardar P, Kolte D, Omer MA, Mahmoud AN, Jneid H, Keeley EC, Bhatt DL. Palliative care use in patients with acute myocardial infarction. *J Am Coll Cardiol* 2020;75:113–117.
5. Elkaryoni A, Chhatriwalla AK, Kennedy KF, Saxon JT, Cohen DJ, Arnold SV. Change in hospitalization rates following transcatheter mitral valve repair: a nationwide cohort sample. *Circ Cardiovasc Interv* 2019;12:e008342.

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Meta-analysis of the Effect of Colchicine on Mortality and Mechanical Ventilation in COVID-19

Due to the significant healthcare and economic burdens of the coronavirus disease 2019 (COVID-19) and the lack of effective treatment, repurposing of existing medications based on plausible mechanism of action have been used. Colchicine, an anti-inflammatory medication, has been proposed as a possible treatment option for COVID-19.

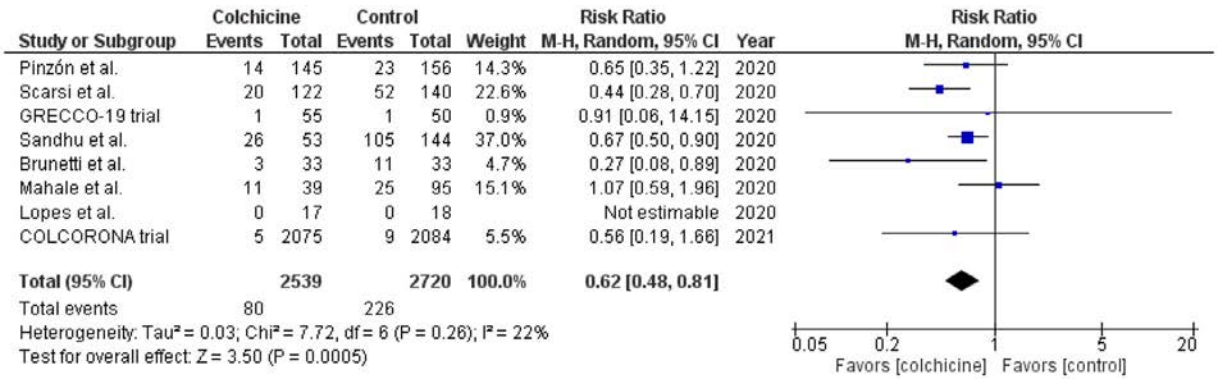

Figure 1. Forest plot examining the association between colchicine use and risk of mortality in patients with COVID-19 infection. CI = confidence interval; M-H = Mantel-Haenszel.

Colchicine exerts its anti-inflammatory effects via inhibition of neutrophil chemotaxis, adhesion, and mobilization; suppression of superoxide production; and reduction of tumor necrosis factor (TNF)-α generation and activity.[1] Additionally, it is proposed that colchicine may have some antiviral properties through inhibition of microtubule polymerization and regulation of production of antioxidative factor.[1–3] Early reports suggested possible benefits for colchicine in patients with COVID-19.[4] Further, a recent meta-analysis showed mortality benefit associated with the use of colchicine in patients with COVID-19.[5] However, since then, more observational studies were published, and the results of the Colchicine Coronavirus SARS-CoV2 Trial (COLCORONA; NCT04322682), the largest clinical trial to date investigating the use of colchicine in non-hospitalized patients with COVID-19 infection, were reported. In this report, we sought to examine the association between colchicine use and severity of COVID-19 infection in the light of the recent evidence.

We searched PubMed and MedRxiv (preprint repository) databases to look for relevant articles using (''colchicine'' and ''COVID-19'') on January 29, 2021. We also searched the bibliographies of relevant articles. Inclusion criteria were: (1) Clinical trial, cohort studies, and case-control studies; (2) Studies included patients with confirmed COVID-19 infection who received colchicine and were compared to patients with confirmed COVID-19 infection who did not receive colchicine; (3) Desired outcomes were reported in the study. No language or time restriction were applied. The desired outcomes were all-cause mortality and mechanical ventilation. The Review Manager software (version 5.4.1, The Cochrane Collaboration) was used for all statistical analyses. Mantel−Haenszel risk ratios and 95% confidence intervals (CIs) were calculated. A random-effects modeling approach was used. Cochran's Q and I^2 index were used for heterogeneity estimation. We considered an I^2 index <25% to be low, an I^2 index between 25% and 80% be moderate, and an I^2 index >80% be high. Sensitivity analysis was done by excluding the studies that were published as preprints. Due to the low number of the included studies (<10), small-study bias was not examined as our analysis was underpowered to detect such bias.

The initial databases query resulted in 132 potential studies. After careful evaluation, only 7 studies met the inclusion criteria.[4,6–11] Review of the bibliographies of relevant articles showed one study available on another database (Research Square) that met our inclusion criteria.[12] Therefore, a total of 8 studies were included with a total of 5,259 patients with COVID-19 infection. About 48.3% of patients in these studies received colchicine. In the mortality analysis, 8 studies were included. Mortality among patients who received colchicine was 3.2%, whereas mortality among those who did not receive colchicine was 8.3%, with a statistically significant difference (RR 0.62; CI [0.48, 0.81]; $I^2 = 22\%$; Figure 1). In the risk of mechanical ventilation analysis, only 5 studied reported this outcome. About 2.4% of the patients who received colchicine required mechanical ventilation, whereas 6.7% of those who did not receive colchicine required mechanical ventilation. However, this difference did

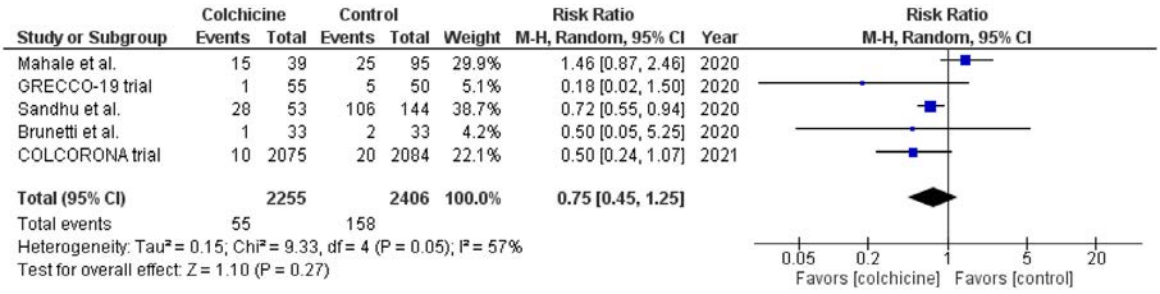

Figure 2. Forest plot examining the association between colchicine use and risk of mechanical ventilation requirement in patients with COVID-19 infection. CI = confidence interval; M-H = Mantel-Haenszel.

not reach statistical significance (RR 0.75; CI [0.45, 1.25]; $I^2 = 57\%$; Figure 2). Sensitivity analysis for both analyses yielded consistent results.

The results of the present analysis show possible mortality benefits associated with the use of colchicine in patients with COVID-19 infection. Although patients who received colchicine tended to have lower risk of mechanical ventilation, the difference between the 2 groups did not reach a statistically significant difference.

There are some limitations of our meta-analysis. First, most of the included studies were observational studies. Second, individual studies had different inclusion criteria and different follow-up periods. Third, there was moderate heterogeneity in the mechanical ventilation analysis. Larger clinical trials are needed to confirm our findings. In this context, several ongoing clinical trials may provide additional information on the safety and efficacy of colchicine in patients with COVID-19 (e.g., NCT04472611, NCT04539873, NCT04667780, and NCT04510038).

Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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1. Schlesinger N, Firestein BL, Brunetti L. Colchicine in COVID-19: an old drug, new use. *Curr Pharmacol Rep* 2020;6:137–145.
2. Jackman RW, Rhoads MG, Cornwell E, Kandarian SC. Microtubule-mediated NF-kappaB activation in the TNF-alpha signaling pathway. *Exp Cell Res* 2009;315:3242–3249.
3. Richter M, Boldescu V, Graf D, Streicher F, Dimoglo A, Bartenschlager R, Klein CD. Synthesis, biological evaluation, and molecular docking of combretastatin and colchicine derivatives and their hCE1-activated prodrugs as antiviral agents. *ChemMedChem* 2019;14:469–483.
4. Deftereos SG, Giannopoulos G, Vrachatis DA, Siasos GD, Giotaki SG, Gargalianos P, Metallidis S, Sianos G, Baltagiannis S, Panagopoulos P, Dolianitis K, Randou E, Syrigos K, Kotanidou A, Koulouris NG, Milionis H, Sipsas N, Gogos C, Tsoukalas G, Olympios CD, Tsagalou E, Migdalis I, Gerakari S, Angelidis C, Alexopoulos D, Davlouros P, Hahalis G, Kanonidis I, Katritsis D, Kolettis T, Manolis AS, Michalis L, Naka KK, Pyrgakis VN, Toutouzas KP, Triposkiadis F, Tsioufis K, Vavouranakis E, Martinèz-Dolz L, Reimers B, Stefanini GG, Cleman M, Goudevenos J, Tsiodras S, Tousoulis D, Iliodromitis E, Mehran R, Dangas G, Stefanadis C. 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:e2013136.
5. Vrachatis DA, Giannopoulos GV, Giotaki SG, Raisakis K, Kossyvakis C, Iliodromitis KE, Reimers B, Tousoulis D, Cleman M, Stefanadis C, Lansky A, Deftereos SG. Impact of colchicine on mortality in patients with COVID-19. A meta-analysis. *Hellenic J Cardiol* 2021 Jan 6. [published online ahead of print].
6. Scarsi M, Piantoni S, Colombo E, Airó P, Richini D, Miclini M, Bertasi V, Bianchi M, Bottone D, Civelli P, Cotelli M-S, Damiolini E, Galbassini G, Gatta D, Ghirardelli M-L, Magri R, Malamani P, Mendeni M, Molinari S, Morotti A, Salada L, Turla M, Vender A, Tincani A, Brucato A, Franceschini F, Furloni R, Andreoli L. Association between treatment with colchicine and improved survival in a single-centre cohort of adult hospitalised patients with COVID-19 pneumonia and acute respiratory distress syndrome. *Ann Rheum Dis* 2020;79:1286–1289.
7. Sandhu T, Tieng A, Chilimuri S, Franchin G. A case control study to evaluate the impact of colchicine on patients admitted to the hospital with moderate to severe COVID-19 infection. *Can J Infect Dis Med Microbiol* 2020;2020:8865954.
8. Lopes MI, Bonjorno LP, Giannini MC, Amaral NB, Benatti MN, Rezek UC, Filho LLE, Sousa BA, Almeida SC, Luppino-Assad R, Veras FP, Schneider A, Rodrigues TS, Leiria LO, Cunha LD, Alves-Filho JC, Cunha TM, Arruda E, Miranda CH, Pazin-Filho A, Martins MA, Borges MC, Fonseca BA, Bollela VR, Del-Ben CM, Cunha FQ, Zamboni DS, Santana RC, Vilar FC, Louzada-Junior P, Oliveira RD. Beneficial effects of colchicine for moderate to severe COVID-19: an interim analysis of a randomized, double-blinded, placebo controlled clinical trial. *medRxiv* 2020. 2020.08.06.20169573.
9. Mahale N, Rajhans P, Godavarthy P, Narasimhan VL, Oak G, Marreddy S, Bedekar A, Dhundi U, Pawar HS, Akole P, Pawar B, Bhurke B, Chavan S, Prayag P, Purandare B, Dalvi P, Telbhare V, Marudwar P, Diwane D, Shahane M, Prayag A, Gugale S, Bhor S, Jog S. A retrospective observational study of hypoxic COVID-19 patients treated with immunomodulatory drugs in a Tertiary Care Hospital. *Indian J Crit Care Med* 2020;24:1020–1027.
10. Brunetti L, Diawara O, Tsai A, Firestein BL, Nahass RG, Poiani G, Schlesinger N. Colchicine to weather the cytokine storm in hospitalized patients with COVID-19. *J Clin Med* 2020;9:2961.
11. Tardif J-C, Bouabdallaoui N, L'Allier PL, Gaudet D, Shah B, Pillinger MH, Lopez-Sendon J, da Luz P, Verret L, Audet S, Dupuis J, Denault A, Pelletier M, Tessier PA, Samson S, Fortin D, Tardif J-D, Busseuil D, Goulet E, Lacoste C, Dubois A, Joshi AY, Waters DD, Hsue P, Lepor NE, Lesage F, Sainturet N, Roy-Clavel E, Bassevitch Z, Orfanos A, Grégoire JC, Busque L, Lavallée C, Hétu P-O, Paquette J-S, Levesque S, Cossette M, Nozza A, Chabot-Blanchet M, Dubé M-P, Guertin M-C, Boivin G. Efficacy of colchicine in non-hospitalized patients with COVID-19. *medRxiv* 2021. 2021.01.26.21250494.
12. Pinzón MA AD, Betancur JF, Holguín H, Arias CA, Muñoz BJ, Amarillo M, Llano JF, Montoya P. Clinical outcome of patients with COVID-19 pneumonia treated with corticosteroids and colchicine in Colombia. *Res Sqaure* 2020.

https://doi.org/10.1016/j.amjcard.2021.02.005