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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 $\sim 7\%$ (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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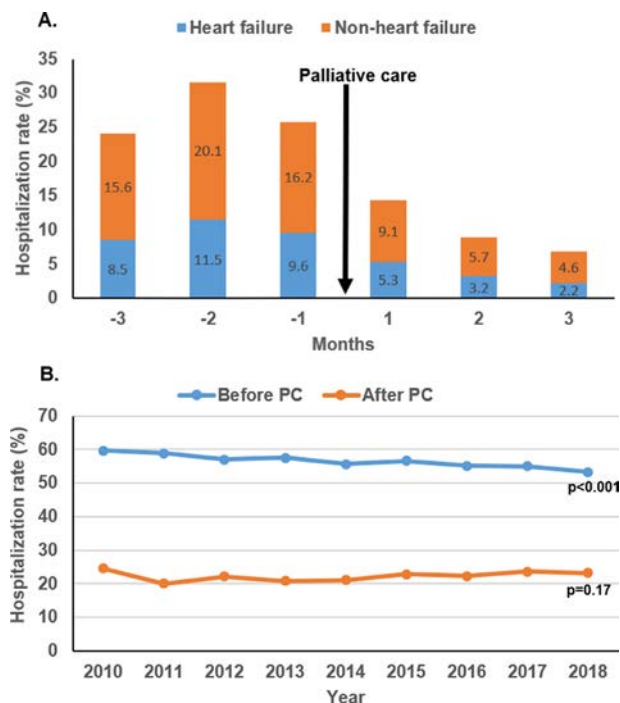


Figure. *Panel A*, Monthly heart failure and non-heart failure hospitalization rates before and after palliative care encounters. *Panel B*, Annual trends of all-cause 90-day hospitalization rates before and after palliative care encounters. PC=palliative care.

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.

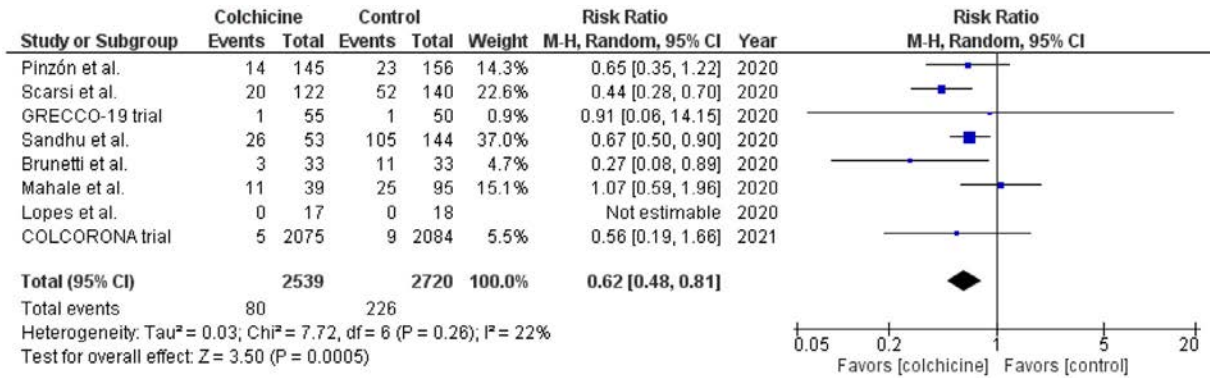


Figure 1. Forest plot examining the association between colchicine use and risk of mortality in patients with COVID-19 infection. CI = confidence interval; M-H = Mantel-Haenszel.

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 I² index were used for heterogeneity estimation. We considered an I² index <25% to be low, an I² index between 25% and 80% be moderate, and an I² 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]; I² = 22%; Figure 1). In the risk of mechanical ventilation analysis, only 5 studies 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

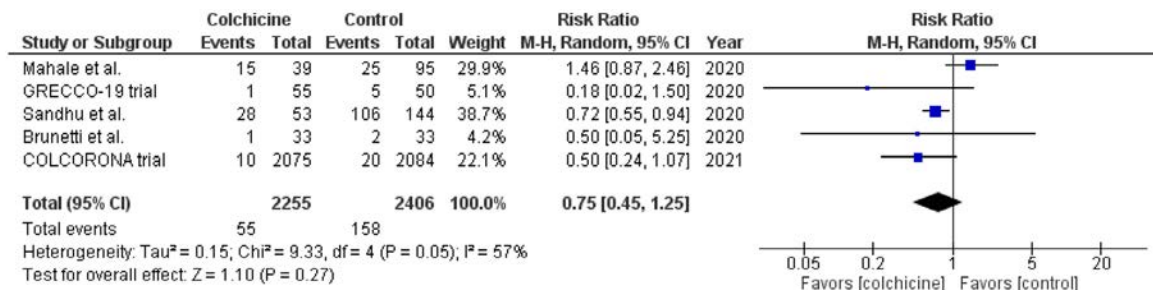


Figure 2. Forest plot examining the association between colchicine use and risk of mechanical ventilation requirement in patients with COVID-19 infection. CI = confidence interval; M-H = Mantel-Haenszel.

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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