

Famotidine and COVID-19 Severity During Hospitalization

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There has been recent speculation surrounding whether famotidine, the active ingredient in a common heartburn medicine, Pepcid, could serve as an antiviral that may inhibit coronavirus replication. A report by Freedberg et al. revealed a decrease in intubation and death in patients who received famotidine upon admission.¹ Our examination of EHR data did not show an obvious difference between the worst severity level of COVID-19 patients who were administered famotidine and those who were not.

This sample consisted of 29,168 active adult patients who were admitted for COVID-19 and had either been discharged or died. Of the admitted COVID-19 patients, 3,345 (11.4%) were administered famotidine, either intravenously or by mouth, within one day of being admitted. As famotidine is often given to patients on a ventilator, for patients who were on ventilators we included them only if they were on famotidine for at least one day before intubation.

As shown in Figure 1, 17% of admitted patients who received famotidine died, compared to 16% who did not receive famotidine. This does not support the finding that famotidine patients experience reduced COVID-19 severity compared to patients not treated with famotidine. Similar results are seen when considering the percent of admitted patients treated with famotidine who required advanced respiratory support or ventilation compared to those not treated with famotidine.

There were 2,970 adult patients who were admitted for COVID-19 but did not have a known outcome (either survived or died), as of May 20, 2020. Of these patients, 485 (16%) were administered famotidine and 2485 (84%) were not. To remain consistent with prior analyses,¹ this sample did not include these patients.

1 Freedberg DE, Conigliaro J, Sobieszcyk M, et al. Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study. *medRxiv*. <https://www.medrxiv.org/content/10.1101/2020.05.01.20086694v2>. Posted May 19, 2020.

Famotidine Administration and Worst COVID-19 Severity n=29,169

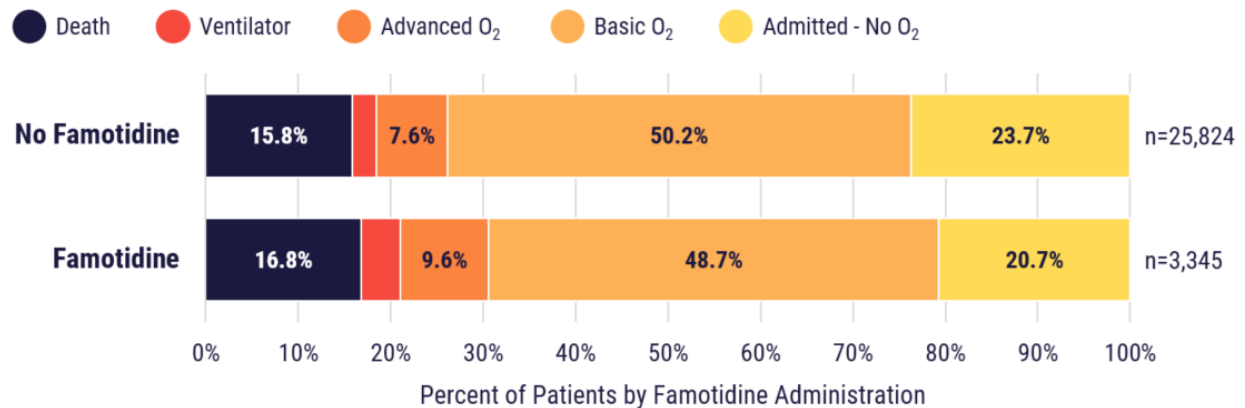


Figure 1: Percent of patients, administered famotidine or not, who reached a specified COVID-19 worst severity.

To see if a possible effect might be hidden by either age or sex, we broke down the data and found that the stratified results were similar to the overall sample. Therefore, it appears that the possible effects of famotidine are not being masked by differences based on age or sex.

Famotidine Administration and Worst COVID-19 Severity n=29,168

by Sex

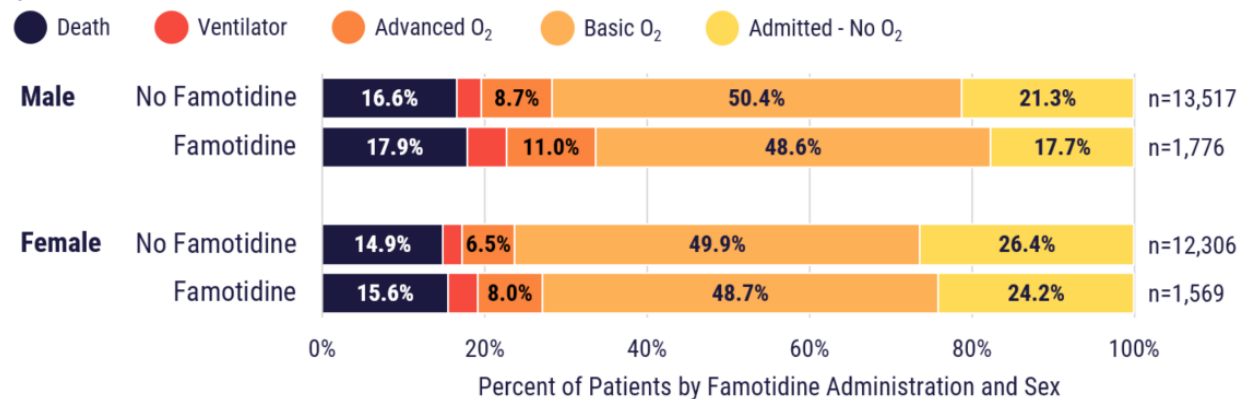


Figure 2: Percent of patients, administered famotidine or not, who reached a specified COVID-19 worst severity, broken down by sex. Note: One patient with a documented sex of “other” in the No Famotidine group was excluded from this graph.

Famotidine Administration and Worst COVID-19 Severity

n=29,169

by Age

● Death
 ● Ventilator
 ● Advanced O₂
 ● Basic O₂
 ● Admitted - No O₂

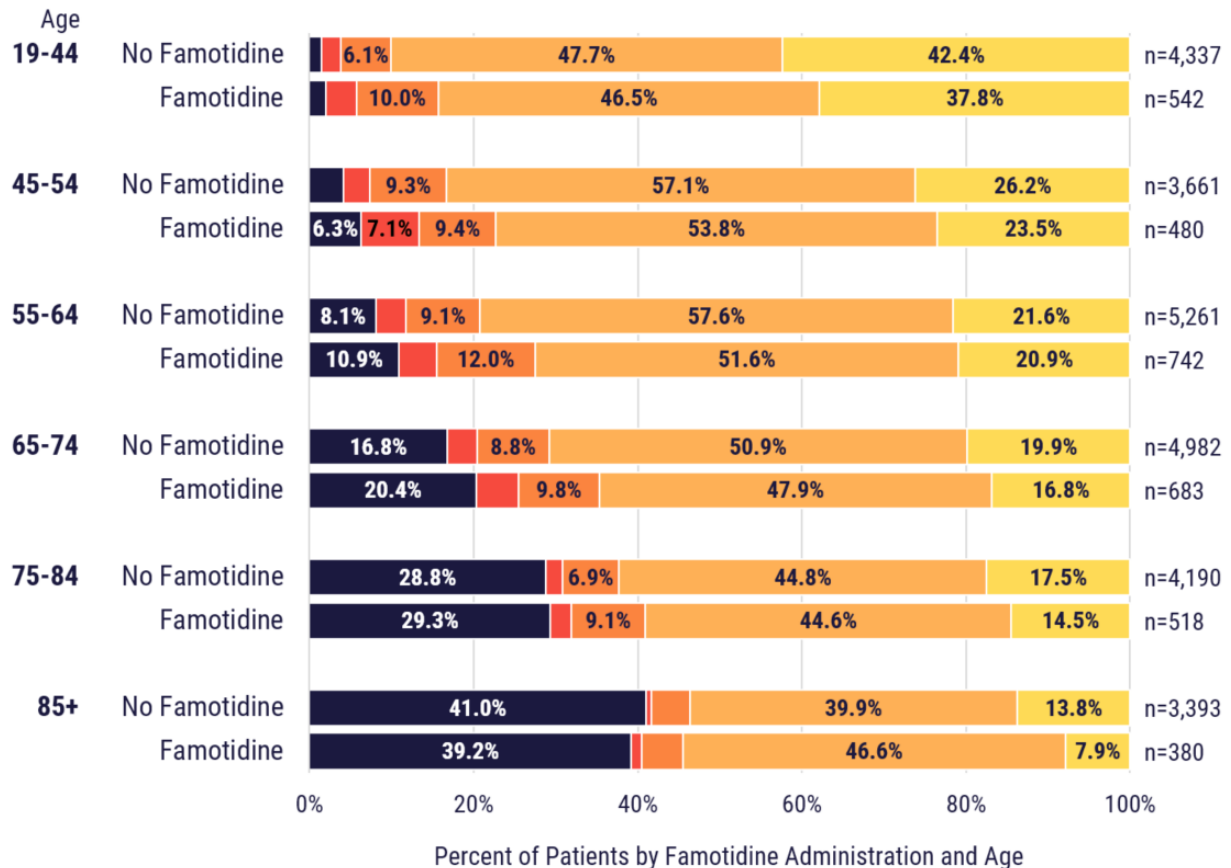


Figure 3: Percent of patients, administered famotidine or not, who reached a specified COVID-19 worst severity broken down by age group.

Further analyses should investigate possible effects of other factors, such as underlying comorbidities, that may prevent seeing an effect from famotidine. For example, it remains possible that patients in our population with other illnesses that were treated with famotidine were more likely to have severe COVID-19 infections, which were mitigated by famotidine.

Data were pooled from electronic medical records at 37 health systems in the United States, spanning 19 states and covering approximately 42 million patients.

Term	Definition
COVID-19 Positive Patient	Patient with a positive SARS-CoV-2 lab result or a COVID-19 diagnosis.
COVID-19 Related Admission	A hospital admission during which the patient has a positive SARS-CoV-2 lab test or COVID-19 diagnosis, OR a hospital admission with any respiratory diagnosis which happens within 14 days of the patient's COVID-19 "start date". Respiratory Diagnosis Codes: J00-J99 (ICD-10)
Ventilator Usage	A patient is considered to be on a ventilator on a day if on any given calendar day there is documentation other than "Off" or a non-invasive mode (e.g. CPAP, BiPAP) in a Vent Mode flowsheet row or an oxygen delivery device of ventilator.
COVID-19 Related Death	A COVID-19 patient with a death date or discharge date with discharge disposition of deceased within 6 weeks of their COVID-19 "start date".
Advanced Respiratory Support	A patient with an O2 flow rate at or above 30 lpm or using a non-invasive ventilator mode or high flow oxygen delivery device (regardless of O2 flow rate) that includes BiPAP, high-flow nasal cannula, T-piece, blow-by, or CPAP if administered between 8am-9pm (to exclude patients who were on nightly CPAP for apnea).
Severity Score Index	<p>An ordinal scale from most severe to least severe:</p> <ul style="list-style-type: none"> • Death • Patient on ventilator • Patient on advanced oxygen support • Patient on basic oxygen support • Patient has COVID-19 related admission, no supplemental oxygen • Discharged • No Admission <p>We have purposefully left our numeric values off our description of this scale. We have aligned this severity scale with the severity index scores used by numerous clinical trials, FDA, CDC, and WHO, regardless of which numeric end they have coded as "high severity".</p> <p>Severity is assessed daily. The most severe score a patient has attained on a calendar date (midnight to midnight) is recorded.</p> <p>Note, if a patient tests positive on Day 0 and is admitted on Day 4, Days 0-3 would be severity=No Admission, Day 4 would be one of the first 5 severity levels. When they are discharged, they would then be severity=Discharged.</p>
Worst Severity	This is defined as the worst severity a patient has attained over all the days assessed for the patient.
Active Patient	A patient who has interacted with the health system in the past 2 years, indicated by either a face-to-face visit or an order placed on their chart.

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<https://ehm.org/wp-content/uploads/Famotidine-and-COVID-19-Severity-During-Hospitalization.pdf>