Effect of Remdesivir on Post-COVID Conditions Among Individuals Hospitalized With COVID-19 by Age

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Conclusions

- RDV treatment was associated with a reduced risk of symptoms and diagnoses related to possible PCC after COVID-19 hospitalization in patients aged <65 and ≥65 years
- More PCC-related symptoms and diagnoses were impacted by RDV treatment, and the effect size tended to be stronger, in the younger age group
- The majority of patients in both age groups did not receive RDV, indicating a missed opportunity for treatment of acute COVID-19 and potential prevention of long-term sequelae of infection
- Long COVID is heterogenous, comprising varied symptoms and conditions. The long COVID outcomes that were diagnoses (eg, neuropsychiatric features) tended to be associated with remdesivir more often than outcomes that were symptoms (eg, fatigue)

Plain Language Summary

People who had COVID-19 may have ongoing health problems that last for weeks, months, or years after infection with SARS-CoV-2, the virus that causes COVID-19. These health problems are referred to as post-COVID conditions or "long COVID." Some examples of long COVID symptoms include tiredness, cough, shortness of breath, difficulty concentrating, loss of taste or smell, joint and muscle pain, heart problems, blood clots, and digestive issues, such as diarrhea. This poster reports the results of a study that used hospital chargemaster data (ie, a list of charges for hospital services) linked to health insurance claims to assess the effect of remdesivir, an antiviral medication used to treat people hospitalized with acute COVID-19, on the later development of long COVID symptoms. The effects of remdesivir were analyzed in 2 age groups: people aged <65 and ≥65 years. The study found that remdesivir treatment lowered the risk of long COVID symptoms after hospitalization for COVID-19 in both age groups.

References: **1.** Centers for Disease Control and Prevention. Long COVID or post-COVID conditions. Accessed January 24, 2024. https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html. **2.** Ford ND, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:866-70. **3.** Notarte KI, et al. *J Clin Med*. 2022;11:7314. **4.** O'Mahoney LL, et al. *EClinicalMedicine*. 2022;55:101762. **5.** Veklury® (remdesivir) injection, for intravenous use [package insert]. Gilead Sciences, Inc.; 2023. **6.** Gilead Sciences, Inc. Veklury 100 mg powder for concentrate for solution for infusion [summary of product characteristics]. Gilead Sciences, Inc.; 2023. **7.** Romero Starke K, et al. *BMJ Glob Health*. 2021;6:e006434. **8.** Dorjee K, et al. *PLoS One*. 2020;15:e0243191.

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Introduction

- Post-COVID conditions (PCC), also referred to as long COVID, are part of a persistent, multisystemic set of symptoms occurring after COVID-19[1]
- The Centers for Disease Control and Prevention reported a PCC prevalence of 6% among all US adults as of June 2023, with a lower long COVID prevalence among the youngest (18-29 years) and the oldest (≥60 years) age groups[2]; however, the association of age with an increased risk of long COVID is not conclusively confirmed in the literature[3]
- PCC include a wide range of respiratory, cardiovascular, neurologic, digestive, and other general symptoms, such as fatigue and joint pain, which may persist for years after SARS-CoV-2 infection[1,2,4]
- Remdesivir (RDV) is an intravenous antiviral approved for the treatment of COVID-19 in nonhospitalized patients at high risk of progression to severe disease and in hospitalized patients[5,6]
- The effect of RDV on subsequent outcomes associated with PCC is unknown. Of particular interest are RDV's effects stratified by age, which is a predictor of general outcomes in patients hospitalized with COVID-19[7,8]

Objective

- To assess the effect of RDV treatment during acute COVID-19 illness on the incidence of PCC-related symptoms and diagnoses in patients aged <65 and ≥65 years hospitalized with COVID-19 in the United States

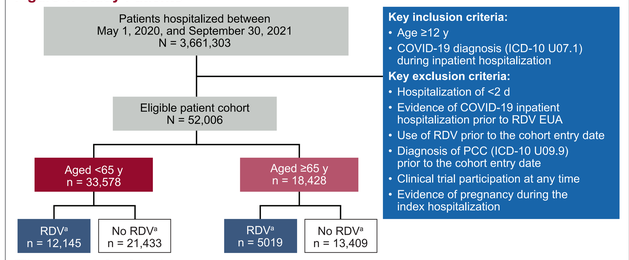
Methods

- Data for this retrospective cohort study were obtained from the HealthVerity database, which provides hospital chargemaster data linked to closed claims
- Individuals aged ≥12 years hospitalized for ≥2 days with COVID-19 between May 1, 2020, and September 30, 2021, were included
- RDV exposure was measured on Day 1 or 2 of hospitalization
- Symptoms and diagnoses associated with PCC that occurred 90 to 270 days post hospitalization were captured using *International Classification of Diseases, Tenth Revision* codes and included:
  - Cognitive dysfunction
  - Cerebrovascular disease
  - Neuropsychiatric features
  - Diarrhea
  - Thromboembolic disease
  - Chest pain
  - Ischemic heart disease
  - Headache
  - Dysautonomia
  - Fatigue
  - Smell disturbance/anosmia
  - Muscle pain/myalgia
  - Taste disturbance/ dysgeusia/ageusia
  - Dyspnea/breathlessness
  - Joint pain/arthralgia
  - Cough
- Follow-up began 2 days after hospital admission and continued until 1 of the following occurred: PCC-related symptom/diagnosis, disenrollment of insurance, death, or maximum follow-up time of 268 days was reached
- Analysis was stratified by age at time of hospitalization (<65 vs ≥65 years)
- Incidence rate per 100 person-years and 95% CIs were calculated for each PCC-related symptom/diagnosis
- Cox proportional hazards models used inverse probability of treatment weighting (IPTW) to calculate hazard ratios (HRs) with 95% CIs for individual PCC-related symptoms/diagnoses and a composite of any PCC-related symptom/diagnosis in patients hospitalized with COVID-19 who received ≥1 administration of RDV within the first 2 days of hospitalization versus comparators who did not receive RDV
  - IPTW adjusted for age, sex, geographic region, pre-existing PCC-related symptoms/diagnoses, COVID-19 disease severity during the first 2 days of hospitalization (oxygen support level, intensive care unit admission, and other treatments), and baseline comorbidities and conditions
- Individuals without ≥90 days of follow-up still contributed person-time up to their day of censoring
- Sensitivity analysis was conducted using IPTW in patients with ≥90 days of follow-up after cohort entry date

Results

- Of the 3,661,303 individuals hospitalized for any reason during the study period, 52,006 patients had acute COVID-19 and met the inclusion criteria (**Figure 1**)
  - 5210 (10%) patients in the full cohort had <90 days of follow-up
- There were 33,578 (65%) patients aged <65 years and 18,428 (35%) patients aged ≥65 years, of whom 12,145 (36%) and 5019 (27%), respectively, received RDV treatment

Figure 1. Study Patients



[a]RDV exposure was measured on Day 1 or 2 of hospitalization.
EUA, emergency use authorization; ICD-10, *International Classification of Diseases, Tenth Revision*; PCC, post-COVID conditions; RDV, remdesivir.

- Baseline demographic and disease characteristics were similar in the RDV and no RDV treatment groups in both age groups, except a higher percentage of patients in the RDV group received corticosteroids, immunomodulators, and/or convalescent plasma on Day 1 or 2 of hospitalization (**Table 1**)

Table 1. Baseline Demographic and Disease Characteristics

Characteristic	Aged <65 y		Aged ≥65 y	
	RDV (n = 12,145)	No RDV (n = 21,433)	RDV (n = 5019)	No RDV (n = 13,409)
Age, y, mean (SD)	50 (11.7)	48 (13.3)	76 (9.4)	78 (10.0)
Sex, n (%)				
Female	5864 (48)	10,566 (49)	2573 (51)	7519 (56)
Male	6281 (52)	10,867 (51)	2446 (49)	5890 (44)
Region, n (%)				
Northeast	2398 (20)	3690 (17)	1269 (25)	3170 (24)
West	3109 (26)	5854 (27)	1230 (25)	3191 (24)
Midwest	659 (5)	1836 (9)	498 (10)	1558 (12)
South	5978 (49)	10,051 (47)	2021 (40)	5487 (41)
Other	1 (<1)	2 (<1)	1 (<1)	3 (<1)
Highest level of oxygen support status on Days 1 and 2 of hospitalization, n (%)				
Room air	7702 (63)	15,809 (74)	3142 (63)	9665 (72)
Low flow	2526 (21)	3135 (15)	1192 (24)	2426 (18)
High flow	1426 (12)	1588 (7)	532 (11)	946 (7)
Invasive	491 (4)	901 (4)	153 (3)	372 (3)
ICU admission on Day 1 or 2 of hospitalization, n (%)	6112 (50)	9881 (46)	2496 (50)	6732 (50)
Medication use on Day 1 or 2 of hospitalization, n (%)				
Corticosteroids	11,588 (95)	11,113 (52)	4709 (94)	6439 (48)
Protease inhibitors	27 (<1)	83 (<1)	9 (<1)	30 (<1)
Immunomodulators	1105 (9)	372 (2)	285 (6)	98 (1)
Convalescent plasma	1387 (11)	368 (2)	683 (14)	292 (2)
Anticoagulants	1904 (16)	5592 (26)	1290 (26)	5100 (38)

ICU, intensive care unit; RDV, remdesivir.

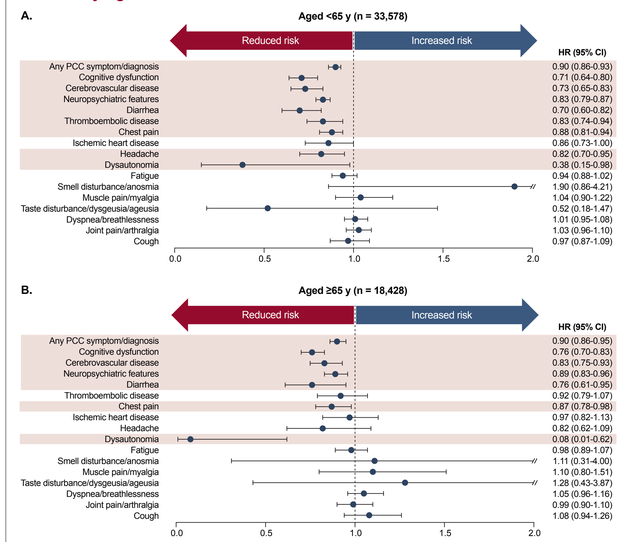
- Following hospitalization, the most common PCC-related symptom/diagnosis, of those assessed in this study, was neuropsychiatric features, with an incidence rate per 100 person-years of 58.0 (95% CI, 56.93-59.03) in patients aged <65 years and 52.3 (95% CI, 50.96-53.62) in patients aged ≥65 years (**Table 2**)
- RDV treatment during the first 2 days of hospitalization (vs no RDV treatment during the first 2 days of hospitalization) was associated with lower relative hazards for any PCC symptom/diagnosis in patients aged <65 years (HR, 0.90 [95% CI, 0.86-0.93]; **Figure 2A**) and in patients aged ≥65 years (HR, 0.90 [95% CI, 0.86-0.95]; **Figure 2B**)
- RDV was associated with lower hazards for 8/16 individual possible PCC-related symptoms/diagnoses in the <65 years age group (**Figure 2A**) and 6/16 individual possible PCC-related symptoms/diagnoses in the ≥65 years age group (**Figure 2B**)
- In the sensitivity analysis among patients with ≥90 days of follow-up, a benefit of RDV on prevention of any symptom was observed in both age groups, with lower hazards for 9/16 individual PCC-related symptoms/diagnoses in the <65 years age group and 5/16 individual PCC-related symptoms/diagnoses in the ≥65 years age group
- In the sensitivity analysis for the <65 years age group, lower hazards were also observed for ischemic heart disease and fatigue but not for dysautonomia; in the ≥65 years age group, a lower hazard was not observed for chest pain

Table 2. Incidence of Individual Possible PCC-related Symptoms and Diagnoses Among Patients Hospitalized With COVID-19, Stratified by Age

Symptom/Diagnosis	Aged <65 y		Aged ≥65 y	
	n	Rate per 100 Person-years (95% CI)	n	Rate per 100 Person-years (95% CI)
Taste disturbance/dysgeusia/ageusia	27	0.1 (0.08-0.16)	14	0.1 (0.06-0.17)
Smell disturbance/anosmia	40	0.2 (0.12-0.22)	10	0.1 (0.04-0.14)
Dysautonomia	35	0.1 (0.10-0.20)	16	0.1 (0.07-0.19)
Muscle pain/myalgia	1042	4.3 (4.03-4.55)	277	2.1 (1.83-2.32)
Headache	1157	4.8 (4.49-5.04)	422	3.1 (2.86-3.46)
Diarrhea	1506	6.2 (5.91-6.54)	679	5.1 (4.73-5.49)
Ischemic heart disease	1323	5.5 (5.17-5.76)	1223	9.3 (8.81-9.86)
Thromboembolic disease	2187	9.2 (8.79-9.56)	1292	9.9 (9.37-10.45)
Cough	2414	10.1 (9.70-10.50)	1314	10.0 (9.48-10.57)
Cerebrovascular disease	2350	9.9 (9.48-10.28)	2873	23.0 (22.22-23.90)
Chest pain	4978	21.5 (20.93-22.13)	2219	17.3 (16.55-17.98)
Cognitive dysfunction	2975	12.6 (12.13-13.04)	4624	39.3 (38.23-40.50)
Joint pain/arthralgia	5444	23.7 (23.09-24.35)	2851	22.5 (21.71-23.36)
Fatigue	5164	22.4 (21.83-23.05)	3598	29.2 (28.24-30.14)
Dyspnea/breathlessness	5923	26.1 (25.42-26.74)	3146	25.1 (24.27-26.03)
Neuropsychiatric features	11,719	58.0 (56.93-59.03)	5899	52.3 (50.96-53.62)

PCC, post-COVID conditions.

Figure 2. Association of RDV With Possible PCC-related Symptoms and Diagnoses, Stratified by Age[a]



[a]Shaded boxes highlight outcomes with lower relative hazards as defined by 95% CIs.
HR, hazard ratio; PCC, post-COVID conditions; RDV, remdesivir.

Limitations

- This analysis utilized hospital chargemaster and medical claims data and therefore may only be generalizable to patients who are insured and who seek medical care
- Certain variables related to COVID-19 infection were not available, including the onset of symptoms relative to hospitalization
- Incidence of PCC-related symptoms/diagnoses may be underestimated since individuals with <90 days of follow-up contributed person-time but only events that occurred between 90 and 270 days were included in the analysis
- The PCC-related symptoms/diagnoses evaluated are not specific to PCC and may be caused by other conditions. Individuals may also have had these conditions at baseline. However, we expect nondifferential misclassification between RDV-treated and untreated groups, and sensitivity analyses excluding patients with PCC symptoms/diagnoses at baseline found similar associations