Remdesivir Effectiveness in Reducing Long-Term Mortality After COVID-19 Hospitalization: A Real-World Analysis

University of Colorado Anschutz Medical Campus

Trisha Agarwal BS, Laurel Beaty MS, Nichole E. Carlson PhD, Adit Ginde MD MPH, Neil Aggarwal MD

University of Colorado School of Medicine, Colorado School of Public Health, Department of Emergency Medicine, Division of Pulmonary Sciences and Critical Care Medicine

BACKGROUND

- COVID-19 continues to carry global morbidity and mortality
- Remdesivir is US FDA approved and currently recommended by the NIH for the early treatment of COVID-19 to prevent disease progression
- The effectiveness of remdesivir on in-patient hospital mortality has been studied with trials such as ACTT-1, Solidarity, and Pinetree
- This is the first study to examine the long-term impact of inpatient remdesivir use (RDV) in survivors of a COVID-19 hospitalization

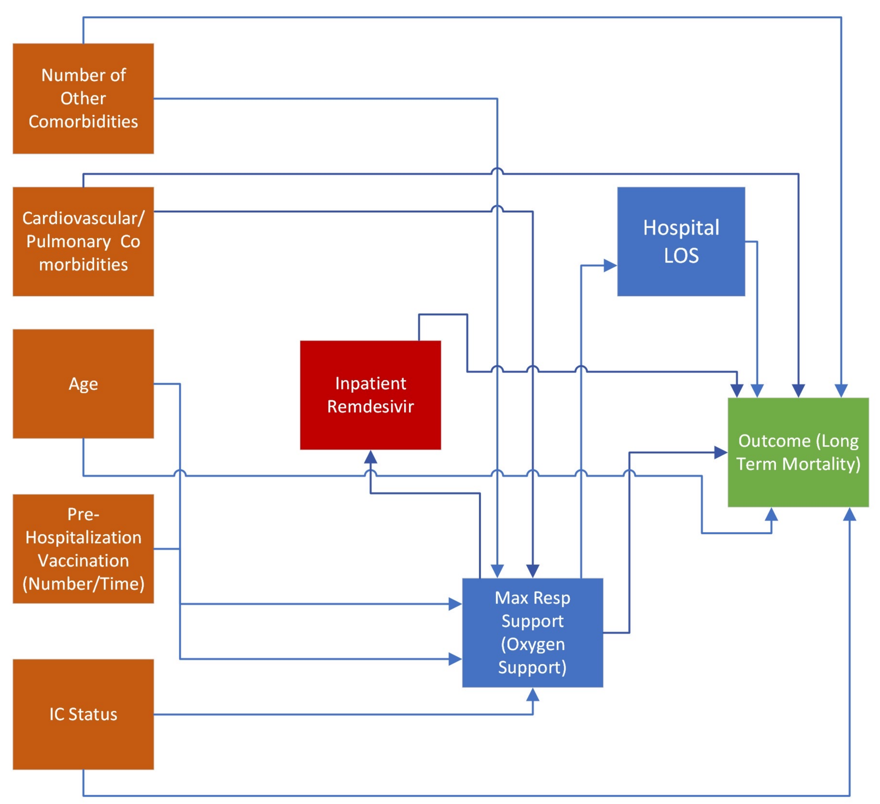
Does inpatient remdesivir use reduce all-cause long-term mortality in patients hospitalized for COVID-19?

METHODS

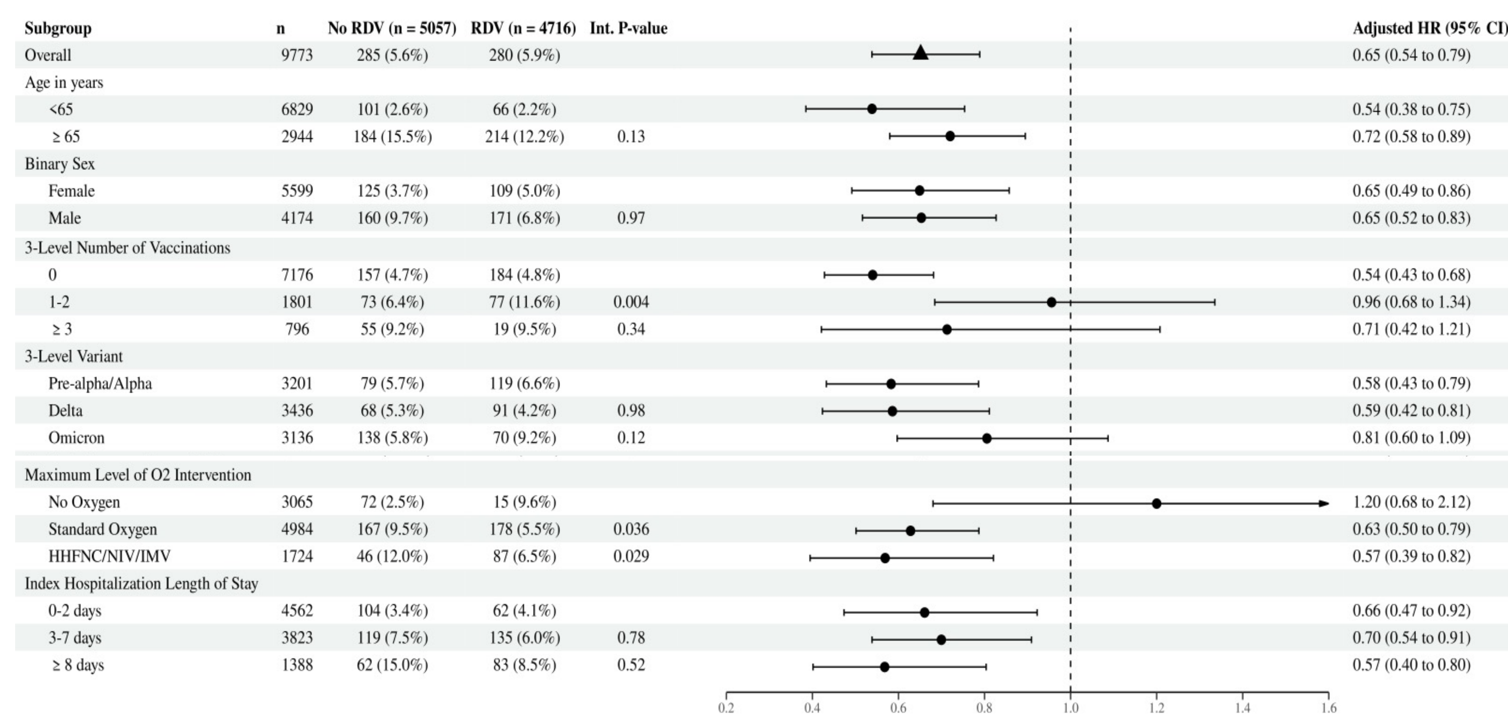
- This is a retrospective cohort evaluating patients who were hospitalized for COVID-19 between November 2020 and October 2022 with at least 6 months of follow up
- Data was collected from three large health centers in Colorado, Utah, and the Colorado Department of Public Health and Environment
- We fit an adjusted cox proportional hazard model for all-cause mortality
- We created a directed acyclic graph to examine mediation and collinearity in the model
- A forest plot was included for cohort sub-groups with associated mortality risk
- A competing risks cox proportional hazard model was used for ED revisits and re-hospitalizations

RESULTS

Directed acyclic graph



Forest plot of cohort sub-groups associated with mortality risk by RDV use



LOS, length of stay; O2, oxygen; HHFNC, heated high flow nasal cannula; NIV, non-invasive ventilation; IMV, invasive mechanical ventilation

Baseline and hospitalization characteristics by RDV use

Characteristic	No RDV (n=4989)	Received RDV (n=4771)
Age Group		
18-44 years	2860 (57.3%)	1194 (25.0%)
45-64 years	980 (19.6%)	1774 (37.2%)
≥ 65 years	1149 (23.0%)	1803 (37.8%)
Female Sex	3362 (67.4%)	2200 (46.1%)
Number of vaccinations prior to SARS-CoV-2+ date		
0	3288 (65.9%)	3889 (81.5%)
1	277 (5.6%)	217 (4.5%)
2	838 (16.8%)	462 (9.7%)
3+	586 (11.7%)	203 (4.3%)
Pre-hospital anti-SARS-CoV-2 Therapy	683 (13.7%)	449 (9.4%)
Pandemic Phase		
Pre-alpha	1019 (20.4%)	1349 (28.3%)
Alpha	347 (7.0%)	481 (10.1%)
Delta	1279 (25.6%)	2173 (45.5%)
Omicron BA.2/BA.2.12.1	1762 (35.3%)	613 (12.8%)
Omicron BA.4/5	582 (11.7%)	155 (3.2%)
Categorical Index Hospitalization LOS		
0-2 days	3003 (60.2%)	1503 (31.5%)
3-7 days	1578 (31.6%)	2277 (47.7%)
8-14 days	258 (5.2%)	650 (13.6%)
≥15 days	150 (3.0%)	341 (7.1%)
Continuous Index Hospitalization LOS (Days)		
Median (IQR)	2 (1-4)	4 (2-7)
Range	0-109	0-115
Maximum Level of O2 Intervention		
No Oxygen	2892 (58.0%)	155 (3.2%)
Standard Oxygen	1709 (34.3%)	3238 (67.9%)
HHFNC/NIV	265 (5.3%)	1083 (22.7%)
IMV	123 (2.5%)	295 (6.2%)

Baseline and hospitalization characteristics by hospitalization survival status

Characteristic	Index Hospitalization Death (n=490)	Index Hospitalization Survival (n=9766)
Age Group		
18-44 years	39 (8.0%)	4056 (41.5%)
45-64 years	125 (25.5%)	2756 (28.2%)
≥ 65 years	326 (66.5%)	2954 (30.2%)
Sex	3414 (67.5%)	2185 (46.3%)
Female	182 (37.1%)	5564 (57.0%)
Number of vaccinations prior to SARS-CoV-2+ date		
0	395 (80.6%)	7182 (73.5%)
1	25 (5.1%)	494 (5.1%)
2	43 (8.8%)	1300 (13.3%)
3+	27 (5.5%)	790 (8.1%)
Pre-hospital mAb or Antiviral Treated	22 (4.5%)	1133 (11.6%)
Pandemic Phase		
Pre-alpha	121 (24.7%)	2369 (24.3%)
Alpha	36 (7.3%)	828 (8.5%)
Delta	247 (50.4%)	3455 (35.4%)
Omicron BA.2/BA.2.12.1	74 (15.1%)	2377 (24.3%)
Omicron BA.4/5	12 (2.4%)	737 (7.5%)
Use of IP RDV	369 (75.3%)	4774 (48.9%)
Maximum Level of O2 Intervention		
No Oxygen	4 (0.8%)	3049 (31.2%)
Standard Oxygen	25 (5.1%)	4951 (50.7%)
HHFNC/NIV	138 (28.2%)	1348 (13.8%)
IMV	323 (65.9%)	418 (4.3%)

Primary and secondary outcomes by RDV use

Outcome	No RDV	RDV	Adjusted HR (95% CI)
Overall Sample Size (n=9773)	**n=4989**	**n=4771**	
All-Cause Mortality	303 (6.1%)	355 (7.4%)	0·73 (0·61-0·87)
Readmitted within 28 days Died prior to readmission	521 (10.4%) 55 (1.1%)	536 (11.2%) 45 (0.9%)	0·77 (0·67-0·89ᵃ)
Bounceback ED visit within 28 days Died prior to ED visit	574 (11·5%) 83 (1.7%)	479 (10.0%) 113 (2.4%)	0·79 (0·67-0·92ᵃ)
Sensitivity Analyses			
All-Cause Mortality	277 (6.7%)	355 (7.4%)	0·73 (0·61-0·88)
Patients re-hospitalized > 6 hours after index hospitalization discharge only (n = 9473)	**n=4874**	**n=4599**	
All-Cause Mortality	279 (5.7%)	305 (6.6%)	0·69 (0·57-0·83)
Readmitted within 28 days Died prior to readmission	406 (8.3%) 55 (1.1%)	364 (7.9%) 45 (1.0%)	0·75 (0·63-0·88ᵃ)
Bounceback ED visit within 28 days Died prior to ED visit	558 (11.4%) 66 (1.4%)	471 (10.2%) 73 (1.6%)	0·80 (0·68-0·93ᵃ)

*Model adjusted by the following variables: age, sex, race/ethnicity, insurance, comorbidities, vaccination status, pre-hospital therapy, pandemic phase, immunocompromised status, length of stay, and oxygen intervention. ICU admission was not included. Precision variables were accounted for in the model using the above directed acyclic graph.

CONCLUSIONS

Remdesivir use may be associated with decreased long-term mortality in survivors of COVID-19 hospitalization.

- RDV use was associated with decreased risk of ED visits and readmissions within 28 days in survivors of COVID-19 hospitalization
- There was heterogeneity of RDV treatment effect on long-term mortality based on vaccination and oxygen status
- Patients that received RDV were older, male, and needed higher oxygen support compared to those that did not receive RDV
- Patients that died during hospitalization received RDV more frequently, were older, more immunocompromised, and hospitalized during the Delta variant compared to patients who survived COVID-19 hospitalization

FUTURE WORK

- Overall, we offer support of the utility of RDV beyond COVID hospitalization in the continued discourse regarding its mortality benefit
- Future considerations will include a new statistical model that will propensity match by RDV use in those that survived and died their COVID-19 hospitalization to address survivor bias and RDV effectiveness at different time points
- In addition, we hope to include additional data including steroid use during hospitalizations and duration of RDV treatment

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