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Mortality is not increased in SARS-CoV-2 infected persons with hepatitis C virus infection

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Abstract

Background: Impact of SARS-CoV-2 infection upon hospitalization, intensive care unit (ICU) admissions and mortality in persons with hepatitis C virus (HCV) infection is unknown.

Methods: We used the Electronically Retrieved Cohort of HCV infected Veterans (ERCHIVES) database to determine the impact of HCV infection upon the rates of acute care hospitalization, ICU admission and all-cause mortality. We identified Veterans with chronic HCV infection and propensity score matched controls without HCV in ERCHIVES. We excluded those with HIV or hepatitis B virus coinfection.

Results: We identified 975 HCV+ and 975 propensity score matched HCV− persons with SARS-CoV-2 infection. Mean FIB-4 score (±SD) was higher in those with HCV (1.9 ± 2.1 vs 1.2 ± 0.9; $P < .0001$) and a larger proportion of those with HCV had cirrhosis (8.1% vs 1.4%; $P < .0001$). A larger proportion of HCV+ were hospitalized compared to HCV- (24.0% vs 18.3%; $P = .002$); however, those requiring ICU care and mortality were also similar in both groups (6.6% vs 6.5%; $P = .9$). Among those with FIB-4 score of 1.45-3.25, hospitalization rate/1000-person-years was 41.4 among HCV+ and 20.2 among HCV−, while among those with a FIB-4 > 3.25, the rate- was 9.4 and 0.6 ($P < .0001$). There was no difference in all-cause mortality by age, gender, FIB-4 score, number of comorbidities or treatment with remdesivir and/or systemic corticosteroids.

Conclusions: HCV+ persons with SARS-CoV-2 infection are more likely to be admitted to a hospital. The hospitalization rate also increased with higher FIB-4 score. However, admission to an ICU and mortality are not different between those with and without HCV infection.

KEYWORDS

COVID-19, ERCHIVES, hepatitis C virus, hospitalization, liver fibrosis, mortality, SARS-CoV-2

1 | INTRODUCTION

The SARS-CoV-2 pandemic has affected nearly every country and territory in the world. The primary target organ for SARS-CoV-2 infection is the respiratory system. However, short- and long-term effects on multiple other organ systems have now been well documented, including effects on cardiovascular,[1] renal,[2] gastrointestinal,[3] hepatic,[3,4] endocrine[5] and neurologic systems.[6,7] Gastrointestinal symptoms have been described in up to 15% of patients and abnormal liver enzymes in up to 36% of the hospitalized

patients.[8,9] Conversely, patients with pre-existing cirrhosis are at a higher risk of liver function deterioration and higher mortality.[10] The effect of hepatitis C virus (HCV) infection upon the severity of SARS-CoV-2 infection is not known. We recently demonstrated that persons with HCV are infrequently tested for SARS-CoV-2 infection with a positivity rate of 6.2% among those who were tested.[11] Several reports have suggested that newer antiviral agents for HCV may also be effective against SARS-CoV-2.[12,13] However, no clinical studies have assessed the impact of HCV upon severity of SARS-CoV-2 illness, rate of hospitalization and mortality compared with an appropriately matched population without HCV infection. We sought to determine these outcomes in a population of Veterans with HCV infection and propensity score matched controls without HCV infection.

Key points

- Persons with HCV and SARS-CoV-2 infection are more likely to be admitted to a hospital.
- The hospitalization rate is higher among those with higher FIB-4 score.
- However, admission to an ICU and mortality are not different between those with and without HCV infection.

2 | METHODS

2.1 | Data sources

We used the Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES) for the current study. Creation of ERCHIVES has been described in numerous previous publications.[11,14-19] Data are updated annually to include Veterans with newly diagnosed HCV and corresponding controls. Briefly, all Veterans with a positive HCV antibody test from 2001 onwards are identified through the VA Corporate Data Warehouse (VA CDW). Age, gender and race matched controls are identified based on a negative HCV antibody test in the same year. Clinical, laboratory, pharmacy, anthropometric and vital signs data are retrieved for each case and control using established definitions and algorithms. Smoking status was retrieved from the Health Factors Dataset (Ref).

2.2 | Definitions

The diagnosis of SARS-CoV-2 infection was confirmed from the VA CDW, where a standard nasopharyngeal swab is tested using RT-PCR to confirm the diagnosis.[11] If multiple tests were done on a single individual, any positive test was considered to be a positive diagnosis for SARS-CoV-2 infection, with first positive test used as the index date. Each individual could be entered into the respective study group only once. Presence of comorbidities was defined using established and published definitions based on International Classification of Diseases, 9th or 10th edition (ICD-9/10) diagnostic codes, laboratory values and/or pharmacy prescription for specific conditions.[14-19] Liver fibrosis stage was calculated using the FIB-4 score using an average of two values closest to, but before baseline. Treatment for SARS-CoV-2 infection was defined as prescription of 2 or more doses of remdesivir or systemic corticosteroids after a positive SARS-CoV-2 test. Smoking status was categorized into current, past or never smoker, as listed in the Health Factors Dataset.

2.3 | Cohort construction

Within the ERCHIVES database, we identified all Veterans with a positive HCV antibody and at least one positive HCV RNA. We excluded those with HIV or HBV coinfection at any time point. For each person with HCV and a positive SARS-CoV-2 test, we identified one propensity score matched control with at least one confirmed negative HCV antibody test or undetectable HCV RNA who remained negative during the duration of recorded follow-up. Propensity score matching was based on age, race, gender, body mass index, and presence of hypertension, diabetes, coronary artery disease, stroke or cancer, smoking status and alcohol use. We used the nearest-neighbour matching (1:1) technique with a calliper of 0.25 standard deviation.

2.4 | Primary outcomes

Primary outcome measures were hospitalization and all-cause mortality. Hospitalization was treated as a binary variable and defined as any admission to an acute care facility that occurred within 14 days after a positive SARS-CoV-2 test. Hospitalization was subdivided into those who were admitted to an acute care unit with no intensive care unit (ICU) stay and those who were admitted or transferred to an ICU setting for any duration of time.

2.5 | Statistical analyses

Baseline characteristics of those with and without HCV were compared using the chi-squared or student's *t*-test, as appropriate. Proportion of persons who were hospitalized without or with any ICU stay was determined and compared for both groups. Mortality rates were calculated and compared for persons with and without HCV overall, and within subgroups by gender, age, comorbidity count, liver fibrosis stage and treatment status. All statistical analyses were completed using SAS Version 9.4 (SAS Institute Inc).

2.6 | Ethical approval

The study was approved by the Institutional Review Board at VA Pittsburgh Healthcare System. A waiver of informed consent requirement has been granted to studies related to ERCHIVES.

3 | RESULTS

Among 237 679 persons with chronic HCV in the ERCHIVES database, 3937 were excluded because of HIV coinfection and 2917 were excluded because of HBV coinfection. Among the remaining 230 825 persons, 17 518 (7.6%) were tested for SARS-CoV-2 and 1095 (6.2% of those tested) had at least one positive test. (Figure 1) Of these, 975 had a propensity score matched HCV uninfected controls, resulting in 975 matched pairs in each group available for final analyses. The groups were well-matched for age, race, gender and presence of comorbidities other than smoking. (Table 1) Mean body mass index (BMI) was similar in both groups (28.5 vs 28.7; $P = .4$) though a larger proportion of those with HCV had a BMI of 25 or lower (28.1% vs 22.5%; $P = .01$). Mean FIB-4 score (±standard deviation, SD) was significantly higher in those with HCV (1.9 ± 2.1 vs 1.2 ± 0.9; $P < .0001$) and a significantly larger proportion of those with HCV had advanced fibrosis or cirrhosis based on a FIB-4 score of >3.25 (8.1% vs 1.4%; $P < .0001$). An equal proportion of persons in both groups received remdesivir, systemic corticosteroids or both. A larger proportion of persons with HCV+ were hospitalized (24.0% vs 18.3%; $P = .002$); however, those requiring ICU care was similar in both groups. Mortality was also similar in both groups (6.6% vs 6.5%; $P = .9$). (Table 1).

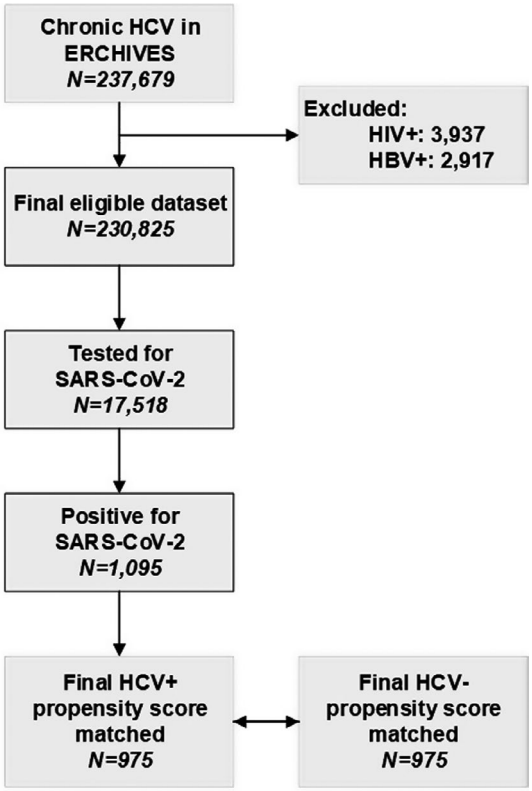

FIGURE 1 Cohort construction and study flow sheet

In subgroup comparisons, there was no difference in hospitalization or ICU admission between those with and without HCV by age, race, gender or presence of comorbidities (Tables 2 and 3). Hospitalization rates were significantly higher among those with HCV who had more advanced liver fibrosis. Among those with a FIB-4 score of 1.45-3.25, hospitalization rates per 1000 person-years were 41.4 among HCV+ and 20.2 among HCV−, while among those with a FIB-4 score of >3.25, the rates were 9.4 and 0.6 ($P < .0001$). Hospitalization with ICU stay were similarly higher in those with FIB-4 score of 1.45-3.25 and >3.25 in persons with HCV (Table 3).

There was no difference in all-cause mortality by age, gender, liver fibrosis score, number of comorbidities or treatment with remdesivir and/or systemic corticosteroids. However, the number of events in each subgroup was relatively small to make meaningful comparisons (Table 4).

4 | DISCUSSION

To our knowledge, this is the first study specifically looking at the impact of HCV infection upon the risk of hospitalization and all-cause mortality compared with a well-matched population without HCV infection, and to assess the impact of liver fibrosis stage upon these outcomes. Overall hospitalization was higher among persons with HCV, but admission to an ICU or all-cause mortality were not different in persons with and without HCV.

Based on earlier studies abnormal liver enzymes are present in 22%-40% of hospitalized patients with SARS-CoV-2 infection and associated with a higher rate of admission to ICU, mechanical ventilation and mortality compared with those with normal liver enzymes.[4,9,20,21] Pre-existing liver disease has been reported in up to 6% of those with SARS-CoV-2 infection, although the exact nature and distribution of these has been rarely reported. Patients with SARS-CoV-2 infection who have pre-existing cirrhosis, 96% require hospital admission or a prolongation of hospital stay and infection is frequently associated with deterioration of liver function and higher mortality.[10] In about one third of the 50 patients in this study, the aetiology of cirrhosis is viral hepatitis.[10] Our study is the largest, and to our knowledge the first study to specifically determine the impact of HCV infection upon hospitalization and mortality rates. We found that a higher proportion of persons with HCV required hospitalization, but there was no difference in the proportion requiring admission or transfer to the ICU or mortality. We carefully matched the groups for age, gender, race and multiple comorbidities. It is well documented that the prevalence of several medical, psychiatric and substance use disorders is different in those with HCV compared with those without HCV[22] and comorbidities are associated with poorer outcomes in persons with SARS-CoV-2 infection. The apparent lack of difference in severity of disease (as measured by the need

TABLE 1 Baseline characteristics of persons with SARS-CoV-2 infection among persons with and without hepatitis C virus infection

	HCV POS	Propensity score matched HCV NEG	
	N = 975	N = 975	
Median age, years (IQR)	52.0 (48,58)	53.0 (48,58)	.32
Race, %			.91
White	29.0%	29.6%	
Black	53.8%	52.6%	
Hispanic	5.8%	5.6%	
Other/Unknown	11.3%	12.1%	
Gender, % male	96.1%	96.8%	.39
Body mass index			
Mean, SD	28.5 (5.5)	28.7 (5)	.45
≤25	28.1%	22.5%	.01
>25-30	37.7%	42.6%	
>30	34.1%	35.0%	
BMI missing			
FIB-4 score			
Mean FIB-4 score (SD)	1.9 (2.1)	1.2 (0.9)	<.0001
FIB-4 < 1.45	47.8%	70.5%	<.0001
FIB-4 1.45-3.25	39.5%	18.8%	
FIB-4 > 3.25	8.1%	1.4%	
FIB-4 missing	4.6%	9.3%	
Comorbidities			
Hypertension	35.8%	35.4%	.85
Diabetes	13.8%	14.1%	.84
Coronary artery disease	6.3%	6.6%	.78
Stroke	1.7%	1.9%	.74
Cancer	3.0%	3.0%	1.00
Smoking			.0004
Current smoker	36.5%	35.0%	
Former smoker	17.7%	15.2%	
Never smoker	14.6%	21.8%	
Unknown	31.2%	28.0%	
Alcohol use disorder	14.0%	12.4%	.28
Treatment			
Remdesivir only	4.9%	4.2%	.45
Systemic corticosteroids only	2.8%	3.0%	.79
Remdesivir + systemic corticosteroids	1.5%	1.4%	.85
Outcomes			
Hospitalized never in ICU	24.0%	18.3%	.002
Hospitalization with any ICU	13.0%	12.5%	.73
Died	6.6%	6.5%	.93

for ICU care) and mortality indicates that any possible differences in these outcomes in persons with and without HCV may be explained, at least in part, by the differential prevalence of these comorbidities.

In subgroup comparisons, the only factor associated with a higher rate of hospitalization or ICU admission in persons with HCV (compared to those without HCV) was more advanced liver fibrosis as measured by the non-invasive FIB-4 score. When comparing those with and without HCV with similar FIB-4 score, the rates of hospitalization and ICU admission were much higher in those with HCV. This indicates that any potential increased risk

TABLE 2 Hospitalization rates per 1000 person-years of follow-up by demographic and clinical factors in patients with SARS CoV-2 infection

	HCV+			HCV−			*P*-value (HCV+ vs HCV−)
	N	Rate (95% CI)	*P*-value (within group)	N	Rate (95% CI)	*P*-value (within group)	
Age							.18
≤60	27	18.5 (12.7,27)	comparator	20	11.5 (7.4,17.9)	comparator	
>60-70	135	18 (15.2,21.4)	.90	88	13.1 (10.7,16.2)	.18	
>70	72	17.6 (14,22.2)	.83	70	13.8 (10.9,17.5)	.03	
Race							.92
White	60	16.6 (12.8,21.3)	comparator	42	11 (8.1,14.9)	comparator	
Black	136	18.6 (15.7,22)	.45	107	14.5 (12,17.5)	.26	
Hispanic	11	12.3 (6.8,22.2)	.37	10	11.3 (6,21)	.32	
Other/Unknown	27	22.7 (15.6,33.1)	.17	19	13.8 (8.8,21.7)	.46	
Gender							.19
Female	5	11.5 (4.7,27.7)	comparator	1	2.4 (0.3,17.3)	comparator	
Male	229	18.2 (16,20.7)	.31	177	13.5 (11.7,15.7)	.18	
Baseline FIB-4 score							<.0001
FIB-4 < 1.45	100	14.7 (12.1,17.9)	comparator	130	13.5 (11.4,16)	comparator	
FIB-4 1.45-3.25	97	20.7 (16.9,25.3)	.02	36	15.4 (11.1,21.4)	.13	
FIB-4 > 3.25	22	27.4 (18,41.6)	.01	1	6.3 (0.8,45.1)	.63	
FIB-4 missing	15	21 (12.6,34.8)	.20	11	8 (4.4,14.5)	.05	
Comorbidities							.31
None	71	14.7 (11.6,18.5)	comparator	60	13.8 (10.7,17.8)	comparator	
1-2	123	17.5 (14.6,20.9)	.24	97	12 (9.8,14.6)	.46	
3 or more	40	34.8 (25.5,47.5)	<.0001	21	19.9 (13,30.5)	.01	

Abbreviation: HCV, hepatitis C virus infection.

of adverse outcomes in persons with HCV is not dependent only on the degree of liver fibrosis. Whether the difference is as a result of viral or host factors is unknown. More studies are needed to understand the true association between HCV and severity of SARS-CoV-2 illness.

Overall mortality was not different between those with and without HCV. In subgroup comparisons, the number of events were generally small in the subgroup to make meaningful comparisons. However, no large numerical differences were apparent by age, gender, liver fibrosis stage or burden of comorbidities.

Treatment for SARS-CoV-2 is a rapidly emerging field. Numerous observational studies and randomized clinical trials have been published assessing the role of antivirals, corticosteroids, IL-6 blockers and other agents. Remdesivir, a nucleoside analogue prodrug with inhibitory effects against several pathogenic animal and human coronaviruses in animal models, including SARS-CoV-2 in vitro, and the Middle East Respiratory Syndrome (MERS) coronavirus, was the first drug approved by the US Food and Drug Administration for the treatment of SARS-CoV-2 infection.[23,24] Systemic corticosteroids have also shown benefit in a subgroups of patients with more severe disease.[25] A very small proportion of persons in our study received remdesivir, systemic corticosteroids or both agents. The number of events among those receiving these agents was too small to make any meaningful comparisons of their effect on mortality.

The strengths of our study include a large national sample, which was carefully matched between the two study groups, racial and geographic diversity of the study population and availability of extensive longitudinal data. Several limitations of our study should also be noted. This was an observational study, and while we carefully matched the groups on propensity scores, there is always a potential for residual confounding. We did not assess the impact of other interventions, including supplemental oxygen use, mechanical ventilation and other potential therapeutic agents. We also did not assess the improvement in symptomatology, oxygen requirements, functional status or other clinical manifestations of SARS-CoV-2 infection.

In conclusion, persons with HCV who develop SARS-CoV-2 infection are more likely to be admitted to a hospital compared with a well-matched group without HCV infection. However, admission to an ICU and mortality are not different between those with and without HCV infection. In subgroup comparisons, those with HCV and advanced fibrosis are more likely to be hospitalized and admitted to the ICU, although no difference in mortality was observed between those with and without HCV and the same degree of liver fibrosis.

TABLE 3 Intensive care unit admission rates per 1000 person-years of follow-up by demographic and clinical factors in patients with SARS CoV-2 infection

	HCV+			HCV−			*P*-value (HCV+ vs HCV−)
	N	Rate (95% CI)	*P*-value (within group)	N	Rate (95% CI)	*P*-value (within group)	
Age							.15
≤60	12	8.2 (4.6,14.5)	comparator	9	5.2 (2.7,10)	comparator	
>60-70	71	9.5 (7.5,12)	.65	56	8.4 (6.4,10.9)	.18	
>70	44	10.8 (8,14.5)	.41	57	11.2 (8.7,14.6)	.03	
Race							.61
White	31	8.5 (6,12.2)	comparator	30	7.8 (5.5,11.2)	comparator	
Black	78	10.6 (8.5,13.3)	.30	74	10 (7.9,12.6)	.26	
Hispanic	6	6.7 (3,14.9)	.59	10	11.3 (6,21)	.32	
Other/Unknown	12	10.1 (5.7,17.8)	.63	8	5.8 (2.9,11.6)	.46	
Gender							.19
Female	4	9.2 (3.4,24.5)	comparator	1	2.4 (0.3,17.3)	comparator	
Male	123	9.8 (8.2,11.6)	.90	121	9.2 (7.7,11)	.18	
Baseline FIB-4 score							.01
FIB-4 < 1.45	64	9.4 (7.3,12)	comparator	86	8.9 (7.2,11)	comparator	
FIB-4 1.45-3.25	49	10.4 (7.9,13.8)	.58	29	12.4 (8.6,17.9)	.13	
FIB-4 > 3.25	9	11.2 (5.8,21.5)	.63	2	12.7 (3.1,50.8)	.63	
FIB-4 missing	5	7 (2.9,16.8)	.52	5	3.6 (1.5,8.8)	.05	
Comorbidities							.51
None	42	8.7 (6.4,11.7)	comparator	33	7.6 (5.4,10.7)	comparator	
1-2	66	9.4 (7.3,11.9)	.69	72	8.9 (7,11.2)	.46	
3 or more	19	16.5 (10.5,25.9)	.02	17	16.1 (10,25.9)	.01	

Abbreviations: HCV, hepatitis C virus infection; ICU, intensive care unit.

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CONFLICT OF INTEREST

All authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

AAB: Study design, data acquisition, data interpretation, writing of the manuscript; PY: Data acquisition, data analysis; RAC: Critical appraisal, data interpretation; OSS: Critical appraisal, data interpretation. Dr Butt had complete access to data at all times and accepts the responsibility of the integrity of this article.

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REFERENCES

1. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(11):1265–1273. https://doi.org/10.1001/jamacardio.2020.3557
2. Kunutsor SK, Laukkanen JA. Renal complications in COVID-19: a systematic review and meta-analysis. *Ann Med*. 2020;52:345-353.
3. Rokkas T. Gastrointestinal involvement in COVID-19: a systematic review and meta-analysis. *Ann Gastroenterol*. 2020;33:355-365.
4. Zarifian A, Zamiri Bidary M, Arekhi S, et al. Gastrointestinal and hepatic abnormalities in patients with confirmed COVID-19: a systematic review and meta-analysis. *J Med Virol*. 2020. https://doi.org/10.1002/jmv.26314
5. Rubino F, Amiel SA, Zimmet P, et al. New-Onset Diabetes in Covid-19. *N Engl J Med*. 2020;383:789-790.
6. Agarwal P, Ray S, Madan A, Tyson B. Neurological manifestations in 404 COVID-19 patients in Washington State. *J Neurol*. 2020. https://doi.org/10.1007/s00415-020-10087-z
7. Romagnolo A, Balestrino R, Imbalzano G, et al. Neurological comorbidity and severity of COVID-19. *J Neurol*. 2020. https://doi.org/10.1007/s00415-020-10123-y
8. Liu J, Cui M, Yang T, Yao P. Correlation between gastrointestinal symptoms and disease severity in patients with COVID-19: a systematic review and meta-analysis. *BMJ Open Gastroenterol*. 2020. https://doi.org/10.1136/bmjgast-2020-000437

TABLE 4 All-cause mortality rate per 1000 person-years of follow-up in various subgroups by HCV status

	HCV+			HCV−			
	N	Rate (95% CI)	*P*-value (within group)	N	Rate (95% CI)	*P*-value (within group)	*P*-value (HCV+ vs HCV−)
Overall	64	4.9 (3.8,6.2)	N/A	63	4.6 (3.6,5.9)	N/A	.78
Males	64	5 (3.9,6.5)	comparator	62	4.7 (3.7,6.1)	comparator	.70
Females	0	No event	N/A	1	2.4 (0.3,17.3)	.51	N/A
Age group							
≤60	2	1.3 (0.3,5.5)	comparator	4	2.3 (0.8,6.1)	comparator	.55
>60-70	26	3.4 (2.3,5.1)	.21	23	3.4 (2.2,5.1)	.46	.97
>70	36	8.8 (6.3,12.2)	.01	36	7.1 (5.1,9.8)	.03	.36
Liver fibrosis stage							
FIB-4 < 1.45	31	4.5 (3.2,6.4)	comparator	44	4.5 (3.4,6.1)	comparator	.98
FIB-4 1.45-3.25	24	5.1 (3.4,7.6)	.67	13	5.5 (3.2,9.6)	.54	.81
FIB-4 > 3.25	6	7.4 (3.3,16.6)	.27	1	6.3 (0.8,45.1)	.75	.88
FIB-4 missing	3	4.2 (1.3,13.0)	.89	5	3.6 (1.5,8.8)	.64	.85
Number of comorbidities							
None	20	4.1 (2.6,6.4)	comparator	20	4.6 (2.9,7.1)	comparator	.73
1-2	32	4.5 (3.2,6.4)	.74	33	4.0 (2.9,5.7)	.66	.66
3 or more	12	10.4 (5.9,18.4)	.01	10	9.4 (5.1,17.6)	.06	.82
COVID-19 treatment							
Neither	52	4.4 (3.3,5.8)	comparator	57	4.6 (3.5,6.0)	comparator	.80
Remdesivir only	9	12.8 (6.6,24.6)	.00	4	6.5 (2.4,17.5)	.50	.27
Systemic corticosteroids only	1	2.6 (0.3,18.8)	.61	1	2.4 (0.3,17.3)	.52	.96
Remdesivir + systemic corticosteroids	2	10.2 (2.5,40.8)	.25	1	4.9 (0.6,35.2)	.95	.56

Abbreviation: HCV, hepatitis C virus infection.

9. Wu Y, Li H, Guo X, et al. Incidence, risk factors, and prognosis of abnormal liver biochemical tests in COVID-19 patients: a systematic review and meta-analysis. *Hepatol Int*. 2020;14:621-637.
10. Iavarone M, D'Ambrosio R, Soria A, et al. High rates of 30-day mortality in patients with cirrhosis and COVID-19. *J Hepatol*. 2020;73(5):1063–1071. https://doi.org/10.1016/j.jhep.2020.06.001
11. Butt AA, Yan P. Rates and characteristics of SARS-CoV-2 infection in persons with hepatitis C virus infection. *Liver Int*. 2021;41(1):76–80. https://doi.org/10.1111/liv.14681
12. Simmons B, Wentzel H, Mobarak S, et al. Sofosbuvir/daclatasvir regimens for the treatment of COVID-19: an individual patient data meta-analysis. *J Antimicrob Chemother*. 2021;76(2):286–291. https://doi.org/10.1093/jac/dkaa418
13. Fu L, Ye F, Feng Y, et al. Both Boceprevir and GC376 efficaciously inhibit SARS-CoV-2 by targeting its main protease. *Nat Commun*. 2020;11:4417.
14. Simon TG, Bonilla H, Yan P, Chung RT, Butt AA. Atorvastatin and fluvastatin are associated with dose-dependent reductions in cirrhosis and hepatocellular carcinoma, among patients with hepatitis C virus: Results from ERCHIVES. *Hepatology*. 2016;64:47-57.
15. Rogal SS, Yan P, Rimland D, et al. Incidence and Progression of Chronic Kidney Disease After Hepatitis C Seroconversion: Results from ERCHIVES. *Dig Dis Sci*. 2016;61:930-936.
16. Li DK, Ren Y, Fierer DS, et al. The short-term incidence of hepatocellular carcinoma is not increased after hepatitis C treatment with direct-acting antivirals: an ERCHIVES study. *Hepatology*. 2018;67:2244-2253.
17. Butt AA, Yan P, Shuaib A, Abou-Samra AB, Shaikh OS, Freiberg MS. Direct-acting Antiviral Therapy for HCV Infection is Associated with a Reduced Risk of Cardiovascular Disease Events. *Gastroenterology*. 2019;156:987-996.
18. Butt AA, Yan P, Aslam S, Shaikh OS, Abou-Samra AB. Hepatitis C Virus (HCV) Treatment With Directly Acting Agents Reduces the Risk of Incident Diabetes: Results From Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES). *Clin Infect Dis*. 2020;70:1153-1160.
19. Butt AA, Yan P, Shaikh OS, Lo Re V, 3rd, Abou-Samra AB, Sherman KE. Treatment of HCV reduces viral hepatitis-associated liver-related mortality in patients: An ERCHIVES study. *J Hepatol*. 2020;73:277-284.
20. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020;382:1708-1720.
21. Zhang G, Zhang J, Wang B, Zhu X, Wang Q, Qiu S. Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a retrospective analysis. *Respir Res*. 2020;21:74.
22. Butt AA, Khan UA, McGinnis KA, Skanderson M, Kent Kwoh C. Comorbid Medical and Psychiatric Illness and Substance Abuse in HCV-infected and Uninfected Veterans. *J Viral Hepatitis*. 2007;14:890-896.
23. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. *N Engl J Med*. 2020;383(19):1827-1837. https://doi.org/10.1056/NEJMoa2015301

24. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 - Final Report. *N Engl J Med*. 2020;383(19):1813-1826. https://doi.org/10.1056/NEJMoa200776
25. Group RC, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMoa2021436

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