

Peer Review File

Article Information: <https://dx.doi.org/10.21037/apm-22-858>

Reviewer A

The article “Need for inpatient rehabilitation and skilled nursing services in COVID-19 patients post hospitalization- a retrospective cohort study” described the retrospective cohort in Michigan about the prognosis after ICU admission and the need of rehabilitation from local experience. The burden of Long COVID rehabilitation has been high despite its mortality has been lowered due to effective vaccination, improved medical care with medical equipment and medications, and a better understanding of COVID-19 and its sequelae. This paper describes an important step in comprehensive care to COVID-19 survivors as majority of us will survive the infection, but may leave with multiple co-morbidities. The author provided solid statistics to describe local experience. However, there are few points I would like the author to clarify / add on:

1. In your introduction, you mentioned the high inpatient mortality worldwide and the enormous burden that it brings to healthcare system. Meanwhile, one of the key reasons of dropped mortality is related to the high efficacy and prevalence of COVID-19 vaccination worldwide¹, apart from a better understanding of COVID-19, improved medical access and medications. Mentioning the efficacy and prevalence of COVID-19 vaccination gives a concrete back drop of shifting our focus from acute disease stage mortality to long term rehabilitation care, since majority of the COVID-19 survivors survived in the later wave, but leaving with multiple morbidities. Therefore, the comprehensive care plan currently should include rehabilitation programs and that should be the key of the time background for this paper. Therefore you may consider to briefly mention the vaccination trend by quoting literatures¹⁻³.

Thank you for the suggestion. We have made changes to the introduction as suggested and added the following text and appropriate references as below (see pages 6,7- Lines 41-49)-

“A number of COVID-19 vaccines are now available worldwide and in the United States the three major types of vaccines are mRNA vaccines, protein subunit vaccines and viral vector vaccines. Two dose mRNA vaccines have been shown to decrease risk of hospitalization by 85% for alpha and delta variants and 65% for the omicron variant. As of August 2022, 67.5% of the world population has received at least 1 dose of the COVID vaccine and 12.51 billion doses have been administered globally. With effective vaccines and better understanding of the

disease process resulting in reduced mortality from COVID-19, the focus is now shifting towards the development of more comprehensive treatment and rehabilitation plans for COVID-19 survivors to minimize the long-term effects of the infection.”

2. In your discussion session line 280, You described the 1-3 months most common symptoms are persistent breathlessness, and fatigue. This is similarly true when we extend the time frame to 9 months. According to a recent meta-analysis⁴, the top 3 symptoms lasting till 9 months are post-activity polypnea (29.8%), shortness of breathe (25.6%) and dyspnoea (15.6). It has been shown that majority of symptoms may resolve till 9 months, for those presenting with more than 9 months, they are more likely to be presented with chronic sequelae of Long COVID-19 Syndrome. You can consider to add this to your discussion part because the rehabilitation program should be long term, and the ultimate goal is the patient could return to pre-morbid status after training. The goal of the rehabilitation program has to be focused and tailored to the individual clinical presentations and underlying pathophysiology, thus this meta-analysis may be useful for your discussion part.

Thank you for the comment and for suggesting the inclusion of this meta-analysis by Yang et al. We have added it to the discussion section of the revised manuscript (see pages 15,16- lines 242-244).

“Another recent meta-analysis reported a wide spectrum of COVID-19 sequelae in previously hospitalized COVID-19 patients with symptoms like fatigue and sleeping disorders persisting up to a year.”

3. In view of the surging need of rehabilitation need worldwide, there have been initial recommendations on what to screen for and how to screen. Some initial and simple investigations / programs have been proposed with regard to individual clinical presentations and underlying pathophysiology⁵. The recommended literature is an initial investigation framework for clinical staff. Would you have any idea to supplement and extend your discussion? You can consider to add this to your discussion and see how your new research can make some insight to our old understanding of rehabilitation program and progress.

Thank you for the comment. This review has now been included in the discussion section of the revised manuscript (see page 17, lines 282-285).

We have added “Yan et al conducted a comprehensive systematic review on Long COVID-19 syndrome and proposed that early identification of targeted populations and early planning of rehabilitations services are vital to the recovery of functional independence and improvement of quality of life in these patients.”

4. It has been noted that some clinically vulnerable patients are included in your studies, do you have their vaccination data? Patients with multiple co-morbidities are more associated with long covid-19 syndrome while previous studies have shown these patients are safe and effective to receive vaccination⁶. It comes to my attention whether you have related data on the special population vaccination data for supplementation, and whether the initial degree of long covid-19 severity is related to their vaccination status in these clinically special population⁷. You can also acknowledge this in your limitation since this may be an upcoming hot trend of investigations in view of aging population worldwide.

Thank you for the comment. While it would certainly be interesting to study how vaccination affects the need for inpatient rehabilitation and skilled nursing services post hospitalization, this is beyond the scope of the current study. COVID-19 vaccination was not available for the majority of the study period and vaccination for elderly became available only towards the end of the study period and hence this data was not collected.

All in all, these are the questions and issues I would like you to address as long COVID is an important topic we face now. I am looking forward to your revision and address the above issue, and adding relevant literature in your paper.

References:

1. Yan ZP, Yang M, Lai CL. COVID-19 Vaccines: A Review of the Safety and Efficacy of Current Clinical Trials. *Pharmaceuticals (Basel)* 2021;14.
2. Arsenault C, Gage A, Kim MK, et al. COVID-19 and resilience of healthcare systems in ten countries. *Nat Med* 2022;28:1314-24.
3. Yin J, Li C, Ye C, et al. Advances in the development of therapeutic strategies against COVID-19 and perspectives in the drug design for emerging SARS-CoV-2 variants. *Comput Struct Biotechnol J* 2022;20:824-37.
4. Yang T; Yan MZ; Li X LE. Sequelae of COVID-19 among previously hospitalized patients up to 1 year after discharge: a systematic review and meta-analysis. *Infection* 2022.
5. Yan Z, Yang M, Lai CL. Long COVID-19 Syndrome: A Comprehensive Review of Its Effect on Various Organ Systems and Recommendation on Rehabilitation Plans. *Biomedicine* 2021;9.
6. Yan Z, Yang M, Lai CL. COVID-19 Vaccinations: A Comprehensive Review of Their Safety and Efficacy in Special Populations. *Vaccines (Basel)* 2021;9.
7. Al-Aly Z, Bowe B, Xie Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 2022.

Reviewer B

Overall, this manuscript topic is timely, and the results provide a unique and important contribution to COVID-19 literature. The aims of the study are clearly

stated, and the methods and results support the topic aims. The large sample size is commendable, but I agree that it is challenging to generalize the findings due to the homogeneity of the population. As you state, your findings, specifically the comorbidities and complications experienced in the hospital setting, can be used to improve facility preparedness and improve efficiency in discharge planning.

Thank you for the encouraging comments. We sincerely appreciate them.

Additional comments and suggestions for minor revisions:

Line 93: add the word “patients” after COVID-19.

Thank you for pointing it out. The correction has been made as suggested by the reviewer.

Table 1: suggest ordering the comorbidities in terms of rank (most prevalent to least prevalent) for ease of readability.

Thank you for the comment. The table 1 has now been modified per the reviewer’s comment for ease of readability.

Briefly describe/define CURB-65.

Thank you for the suggestion. The definition of CURB-65 has been added to the methods sections of the manuscript. (see pages 9.10- Lines 108-112)

We have added to the manuscript “CURB-65 is clinical prediction score helpful in predicting mortality in patients with community acquired pneumonia or suspected infection. It is calculated based upon presence of the following: confusion, blood urea nitrogen >7 mmol/l, respiratory rate ≥ 30 , blood pressure (systolic <90 mm Hg or diastolic ≤ 60 mm Hg) and age ≥ 65 years. Higher CURB-65 score indicates higher risk of mortality”.

Reference-

Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, Macfarlane JT. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003 May;58(5):377-82. doi: 10.1136/thorax.58.5.377.

Suggest making a clearer connection between the impact/correlation of length of stay at the ICU level of care and discharge disposition. Comment to the specific length of stay in the ICU for individuals and their discharge disposition, instead of just saying “those with a longer length of stay”. Additionally, if the data is at all available, I would be curious to know a general functional status of individuals discharging to home from the hospital. In my experience, during the height of the pandemic waves, individuals requiring a high burden of care were more likely to be discharged home instead of another facility due to many factors. You do mention differences in Michigan vs NY discharge restrictions, but I was curious if you’ve had a similar

experience of individuals, who may have previously qualified for inpatient rehab, were now deciding to discharge to home.

Thank you for the comment. Unfortunately, the data on general functional status of the individuals could not be reliably collected from the electronic medical records. This limitation has now been added to the discussion section of the revised manuscript. (see page 18, line 297)

We do acknowledge that there is a possibility that some of the patients who were recommended discharge to inpatient rehabilitation or skilled nursing facility might have refused the recommendation and chosen to be discharged home. This has already been mentioned as one of the limitations of the study in the discussion section of the manuscript. (see page 18, Line 294-295)

Regarding the length of stay, it was coded as a continuous variable in the analysis. Upon regression analysis, length of stay OR value of 1.07; 95% CI, 1.04-1.11; $p < 0.001$ indicates that for each additional day the patient needed to stay in the hospital, the odds of discharge to a facility increased by 7%. The detailed results of the regression model for all the significant factors (including length of stay) have already been mentioned in the results section of the manuscript and the table 3. For more clarity, we have further added the following to the results section of the revised manuscript "For each additional day the patient needed to stay in the hospital, the odds of his discharge to a facility increased by 7%" (see page 14, Line 206-207)

Ensure the use of active voice throughout the manuscript. Suggest reviewing the document for passive voice. For example, line 281 "It has been recommended..." Thank you for pointing it out. It has now been corrected in the manuscript.

Reviewer C

I have carefully read your article proposal and have considered making the following clarifications:

1. As it deals with scientific content, the expression "black population" may be considered by some readers as inappropriate. Although not strictly necessary, I suggest you change it to "afroamerican" or something less controversial.

Thank you for the suggestion. However, we have adhered to the guidelines published by Journal of American Medical Association (JAMA) on how to report race in the scientific literature. Since the patient population in our study may have different ancestry and may not identify themselves as African American, we have used the race as Black (as recommended by JAMA).

“The terms African American or Black may be used to describe participants in studies involving populations in the US, following how such information was recorded or collected for the study. However, the 2 terms should not be used interchangeably in reports of research unless both terms were formally used in the study, and the terms should be used consistently within a specific article. For example, among Black people residing in the US, those from the Caribbean may identify as Black but not as African American, whereas Black people whose families have been in the US for several generations may identify as Black and African American. When a study includes individuals of African ancestry in the diaspora, the term Black may be appropriate because it does not obscure cultural and linguistic nuances and national origins, such as Dominican, Haitian, and those of African sovereign states (eg, Kenyan, Nigerian, Sudanese), provided that the term was used in the study”

Reference-

Flanagin A, Frey T, Christiansen SL, AMA Manual of Style Committee. Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals. *JAMA*. 2021;326(7):621–627. doi:10.1001/jama.2021.13304

2. You write about the second wave of the COVID-19 pandemic in the State of Michigan, but considering that the temporal distribution of the "waves" has not been the same around the world, I suggest you include information about the covid-19 variant predominant in the second wave in Michigan (original, omicron, delta...) and you show bibliography about it.

Thank you for the suggestion. During the initial period of this study (October 1, 2020 to mid Jan,2021) the original variant of SARS-CoV-2 was predominant in Michigan. The first case of Alpha variant (B.1.1.7) in Michigan was identified on January 16, 2021. Thereby, the study includes the patients affected by original or alpha variant of the SARS-CoV-2 virus. This information has now been added to the methods section of the revised manuscript (see page 8, Lines 81-84)

3. You use abbreviations of health services typical of the United States health system (SNF, IRF, AFC...). It would be convenient if you described the full name and what each of these services consists (treatments, staff, criteria for referral of patients...).

Thank you for the comment. All the abbreviations have been defined in the methods section of the manuscript. (see page 9, lines 103-104).

The additional information about the criteria for discharge is as per the Centers for Medicare and Medicaid Services guidelines for discharging patient to a facility. The appropriate reference has been added to the manuscript. (see page 10, line 124-125)

4. Taking into account the high number of homeless people in the USA, when you describe "home" you must identify if the patient really has a home (building) or is homeless and returns/enters from "the street".

Thank you for the comment. The data for the discharge disposition was collected from the electronic medical records. Per the discharge summary, a patient is discharged 'home' if their medical condition does not warrant additional need for inpatient skilled services. Although it would be interesting to see the effects of social determinants of health such as being home-less on the discharge disposition, however the current study did not focus on that detail. We have mentioned in the methods section of the manuscript that 'In a small number of patients for whom, the admission or discharge disposition could not be reliably collected from the records, it was mentioned as unknown.' (see page 10, line 127-128)

According to the national data on homeless population in U.S, about 0.2% of US population is homeless. However, in the state of Michigan where this study was conducted, there are less than 10 homeless individuals per 10,000 people (so less than 0.001%). In our study, discharge disposition of about 4.5% was unknown. Hence, we believe this unknown group would have captured any individuals with a homeless status.

Reference: <https://www.nhipdata.org/local/upload/file/The-State-of-Homelessness-in-America.pdf>

5. Although the conclusions are ok, it would be interesting to explain what implications for future practice can be drawn from the study.

The conclusion section has been modified as per the suggestion from the reviewer. (see page 18,19- lines 307-309)

We have added "The information regarding utilization of these services can assist further research on appropriate resource allocation for future pandemic preparedness."