

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comorbidities, symptoms, and end-of-life medication use in hospitalized decedents before and during the COVID-19 pandemic: a retrospective regional cohort study in Ottawa, Canada
AUTHORS	Lawlor, Peter; Cohen, Leila; Adeli, Samantha; Besserer, Ella; Gratton, Valérie; Murphy, Rebekah; Warmels, Grace; Bruni, Adrianna; Kabir, Monisha; Noel, Chelsea; Heidinger, Brandon; Anderson, Koby; Arsenault-Mehta, Kyle; Wooller, Krista; Lapenskie, Julie; Webber, Colleen; Bedard, Daniel; Enright, Paula; Desjardins, Isabelle; Bhimji, Khadija; Dyason, Claire; Iyengar, Akshai; Bush, Shirley H.; Isenberg, Sarina; Tanuseputro, Peter; Vanderspank-Wright, Brandi; Downar, James; Parsons, Henrique

VERSION 1 – REVIEW

REVIEWER	Yamamoto, Takanori Nagoya University Graduate School of Medicine Faculty of Medicine
REVIEW RETURNED	19-Jun-2023

GENERAL COMMENTS	<p>I think this was a valuable and unique paper on palliative care therapy for COVID-19 patients. The finding that opioid and sedation use increases in critical care settings, especially in COVID-19 patients, was groundbreaking. As a discussion, it was noted that many patients with COVID-19 have severe dyspnea and many have cognitive impairments. I think that consideration is generally valid.</p> <p>However, if this is the case, why do COVID-19 patients have a smaller proportion of those on mechanical ventilators than the other two patient groups? Patients with severe dyspnea are generally treated with high-flow nasal canal, BIPAP, and mechanical ventilation. The more severe the dyspnea, the more likely the patient is to receive mechanical ventilator therapy.</p> <p>In addition, during the COVID-19 pandemic, intensivists and intensive care nurses had to wear personal protective equipment to enter the rooms, many facilities had to rush to create isolation rooms, and more medical personnel were needed than for other patients, so they were not able to see patients as closely and quickly as usual. The situation was such that they could not rush to the patients immediately.</p> <p>Thus, there was concern that if patients became delirious, they would not be able to respond immediately. Therefore, It is possible that the dosage of opioids and sedatives was increased.</p>
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	I think the study would be more in-depth if these perspectives are also included.
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REVIEWER	Chee , Marcel Lucas Monash University, Faculty of Medicine, Nursing and Health Sciences
REVIEW RETURNED	17-Jul-2023

GENERAL COMMENTS	<p>Thank you for the opportunity to review the manuscript titled "Comorbidities, symptoms, and end-of-life medication use in hospitalized decedents before and during the COVID-19 pandemic: a retrospective regional cohort study ". I would like to commend the authors on the well-conducted study and its clear presentation. I find the manuscript to be of high quality and suitable for publication in its current form.</p> <p>The objectives of the study are well defined, the statistical analysis is appropriate, the methodology is clear and detailed, and outcomes are thoroughly described. The study provides a clear summary of the clinical characteristics such as comorbidities and symptoms among COVID-19 decedents. The study also compares the end-of-life palliative medication use between pre-pandemic, COVID-ve, and COVID+ve decedents, which can inform the evolving best practice of end-of-life symptom management in COVID-19 patients and in future pandemics.</p> <p>The authors also acknowledge the limitations of the study, particularly its retrospective nature and the lack of standardized symptom assessment. Conclusions such as "our results suggest that respiratory distress mediated higher opioid use in the COVID+ve group, particularly in ICU decedents" are framed in light of these limitations and are justified by sound statistical analysis and references to the existing literature. Overall, there is balanced discussion and measured inferences from the data.</p> <p>In conclusion, I believe the study significantly adds to the understanding of end-of-life care for COVID-19 patients and provides insight into the unique challenge of end-of-life symptom management, especially in ICU settings. I recommend the acceptance of manuscript for publication, and thank you again for the opportunity to review this manuscript.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Takanori Yamamoto, Nagoya University Graduate School of Medicine Faculty of Medicine

Comments to the Author:

I think this was a valuable and unique paper on palliative care therapy for COVID-19 patients. The finding that opioid and sedation use increases in critical care settings, especially in COVID-19 patients, was groundbreaking. As a discussion, it was noted that many patients with COVID-19 have severe dyspnea and many have cognitive impairments. I think that consideration is generally valid.

Author response: thank you, Dr Yamamoto

1(a) However, if this is the case, why do COVID-19 patients have a smaller proportion of those on mechanical ventilators than the other two patient groups? Patients with severe dyspnea are generally treated with high-flow nasal canal, BIPAP, and mechanical ventilation. The more severe the dyspnea, the more likely the patient is to receive mechanical ventilator therapy.

1(a) Author response: thank you for highlighting this and other potential pandemic-related logistical constraints for our attention. We acknowledge that fewer COVID+ve group decedents received mechanical ventilation during their admission: 16.5% versus 26.5% and 25.3% in the Pre-COVID and COVID-ve groups, respectively, albeit not statistically significant. We agree that generally the more severe the level of dyspnoea, the more likely the patient will receive mechanical ventilation. However, the decision-making process was likely influenced by service capacity constraints and the goals of care; these data were not retrieved in our retrospective review.

We have responded to this and the other Reviewer 1 concerns by introducing a whole new paragraph in the discussion section. We feel strongly that we should not speculate too much in the absence of data. However, we state the possibility that a choice was made to use more opioid and/or sedative medication in some of the patients in the COVID+ve group rather than resort to mechanical ventilation.

1(b) In addition, during the COVID-19 pandemic, intensivists and intensive care nurses had to wear personal protective equipment to enter the rooms, many facilities had to rush to create isolation rooms, and more medical personnel were needed than for other patients, so they were not able to see patients as closely and quickly as usual. The situation was such that they could not rush to the patients immediately.

1(b) Author response:

We have addressed this concern in the second sentence of the newly inserted paragraph. This sentence reads: "It is also possible that more rigorous and prompt assessment of those dying of COVID-19 could have been impeded to some extent by isolation requirements and the need for staff to don burdensome personal protective equipment; this could have resulted in greater reliance on opioids and sedatives for symptom management."

1(c) Thus, there was concern that if patients became delirious, they would not be able to respond immediately. Therefore, It is possible that the dosage of opioids and sedatives was increased.

1(c) Author response: rather than focus on the immediate temporal response of staff to a delirious patient (we don't have specific data on this), we feel it is wiser to emphasize the issue of adequate assessment and the fact that the pandemic's restrictions broadly might have impeded adequate assessment of delirium, which in turn might have impacted pharmacological management. Please also note that we have highlighted the lack of end-of-life assessment information already: the second sentence of the Study Strengths and Limitations reads: "The retrospective design and use of admission symptom assessment and comorbidity data without similar data, including medication efficacy and side-effects, from within the more immediate end-of-life period are obvious limitations".

1(d) I think the study would be more in-depth if these perspectives are also included.

1(d) Author response: we trust that our edits have addressed the reviewer's concerns

Reviewer: 2

Dr. Marcel Lucas Chee, Monash University

Comments to the Author:

Thank you for the opportunity to review the manuscript titled "Comorbidities, symptoms, and end-of-life medication use in hospitalized decedents before and during the COVID-19 pandemic: a retrospective regional cohort study ". I would like to commend the authors on the well-conducted study and its clear presentation. I find the manuscript to be of high quality and suitable for publication in its current form.

The objectives of the study are well defined, the statistical analysis is appropriate, the methodology is clear and detailed, and outcomes are thoroughly described. The study provides a clear summary of the clinical characteristics such as comorbidities and symptoms among COVID-19 decedents. The study also compares the end-of-life palliative medication use between pre-pandemic, COVID-ve, and COVID+ve decedents, which can inform the evolving best practice of end-of-life symptom management in COVID-19 patients and in future pandemics.

The authors also acknowledge the limitations of the study, particularly its retrospective nature and the lack of standardized symptom assessment. Conclusions such as "our results suggest that respiratory distress mediated higher opioid use in the COVID+ve group, particularly in ICU decedents" are framed in light of these limitations and are justified by sound statistical analysis and references to the existing literature. Overall, there is balanced discussion and measured inferences from the data.

In conclusion, I believe the study significantly adds to the understanding of end-of-life care for COVID-19 patients and provides insight into the unique challenge of end-of-life symptom management, especially in ICU settings. I recommend the acceptance of manuscript for publication, and thank you again for the opportunity to review this manuscript.

2 Author response: thank you, Dr Lucas