Research

Comparison of health-related quality of life after intensive care in patients before versus during the COVID pandemic

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ABSTRACT

Background: Health-related quality of life (HRQL) is commonly reduced after critical illness and intensive care unit (ICU) stay. The coronavirus disease (COVID-19) pandemic challenged regular medical standards, potentially influencing HRQL post-ICU patients. However, whether patients treated in the ICU due to COVID-19 report worse or better HRQL compared to patients admitted to the ICU before the pandemic is unclear and remains to be evaluated

Aim: To evaluate HRQL after ICU stay in COVID-19 patients compared with patients admitted to the ICU before the pandemic.

Methods: A single center cohort study included all adult patients admitted to the ICU at a tertiary care hospital in Stockholm, Sweden due to acute COVID-19 infection during 2020–2021 with HRQL data at 4-9 months after ICU discharge. For comparison, patients admitted to the ICU for a minimum of 72 hours during 2018-2019 with HRQL data at 6 months post-ICU were included. HRQL was assessed with the RAND-36 questionnaire. Linear regression was performed to assess the differences in RAND-36 scores between groups, also adjusting for potential confounders.

Results: The study included a total of 164 COVID-19 patients and 105 non-COVID-19 patients. COVID-19 patients were younger, had lower Simplified Acute Physiological Score 3 scores and longer duration of mechanical ventilation, with a smaller proportion receiving mechanical ventilation. There were no statistically significant differences in reported HRQL post-ICU between the groups, after adjusting for confounders.

Conclusion: HRQL did not differ between ICU patients admitted before and during the pandemic. The impact of circumstances during the pandemic may have been less

significant than expected. Identification and follow-up of post-ICU symptoms is relevant for ICU survivors irrespective of the initial diagnosis.

Keywords: critical care, COVID-19, intensive care unit, pandemics, quality of life

INTRODUCTION

For many patients, the intensive care unit (ICU) stay is an unexpected, life-altering experience that impacts their physical and psychological health and cognitive and social functioning for months to years after their critical care (Desai, Law & Needham, 2011). Several studies demonstrate that ICU stay contributes to lower health-related quality of life (HRQL) compared to patients' pre-ICU status and compared to a matched general reference population (Desai, Law & Needham, 2011; Gerth, Hatch, Young & Watkinson, 2019). The decreased HRQL is reported to be contributed by comorbidities as well as lingering post-ICU complications, such as post-intensive care syndrome (PICS), with a range of physical, psychological and cognitive impairments (Desai, Law & Needham, 2011; Gerth, Hatch, Young & Watkinson, 2019; Myers, Smith, Allen & Kaplan, 2016). These impairments pose challenges for ICU survivors to return to their former lives (Desai, Law & Needham, 2011; Gerth, Hatch, Young & Watkinson, 2019; Myers, Smith, Allen & Kaplan, 2016).

The coronavirus disease (COVID-19) pandemic introduced a completely new, quickly spreading disease, and an extreme number of patients requiring intensive care, challenging regular medical standards in the ICU. Survivors of COVID-19 have reported lingering symptoms and complications, such as respiratory problems, fatigue and brain fog, often referred to as long-term COVID-19 (Raveendran, Jayadevan & Sashidharan, 2021). These problems can persist for months after acute illness and could have influenced HRQL in COVID-19 patients (Taboada et al., 2022; Gamberini et al., 2021; Figueiredo et al., 2022; Vlake et al., 2021a; Rousseau et al., 2021).Despite many aspects of COVID-19 on HRQL still being unclear, some previous studies have demonstrated that COVID-19 patients treated in the ICU reported lower HRQL after ICU stay compared to their pre-ICU status and compared to hospitalized COVID-19 patients not treated in the ICU (Taboada et al., 2022; Gamberini et al., 2021; Figueiredo et al., 2022).

Various characteristics and consequences of the COVID-19 pandemic differ from regular intensive care and could contribute to reduced HRQL in COVID-19 patients. Firstly, the severity of COVID-19 respiratory symptoms and the potential long-term effects on respiratory function, coupled with the unique circumstances of intensive care during the pandemic, might have played a crucial role. Secondly, patients admitted to the ICU due to COVID-19 experienced longer stays than regular ICU patients and required extended time with mechanical ventilation, potentially resulting in negative outcomes and long-lasting effects on patients' HRQL (Figueiredo et al., 2022; Domazet Bugarin et al., 2023; Cijs et al., 2023). Finally, psychosocial stressors linked to the pandemic, such as the fear of infection, social isolation and the emotional burden of the situation, may have contributed to variations in HRQL between COVID-19 survivors and patients treated before the pandemic (Vlake et al., 2021b).

Previous results on COVID-19 patients' outcomes are conflicting, and comparisons with patients admitted before the pandemic are lacking (Figueiredo et al., 2022; Domazet Bugarin et al., 2023; Cijs et

al., 2023). It is currently unknown whether patients treated in the ICU due to COVID-19 report worse or better HRQL compared to patients admitted to the ICU before the pandemic.

AIMS

The aim of this study was to evaluate HRQL after ICU stay in COVID-19 patients and compare their HRQL with patients admitted to the ICU before the pandemic.

METHODS

Study design and patient selection

This study was a single-center cohort study conducted at a tertiary care hospital in Stockholm, Sweden (Södersjukhuset), with a total of approximately 500 beds across the entire hospital. Before the pandemic, the hospital had 16 ICU beds. During the COVID-19 waves, capacity was temporarily increased up to 60 beds depending on need, before returning to the original 16 beds. All adult patients admitted due to COVID-19 infection during 2020-2021, who completed the 36-item health-related quality of life questionnaire (RAND-36) at four to nine months after ICU discharge, were included. All COVID-19 patients were confirmed with a positive PCR test for COVID-19. For comparison, all adult patients admitted to the ICU for a minimum of 72 hours during 2018–2019, with 6-month RAND-36 data, were included.

Ethical approval for the study was granted by the Swedish Ethical Review Authority, record number 2022-03531-02.

Data collection

Data on patient characteristics

Data on patients treated due to COVID-19 during 2020–2021 were collected from the electronic medical record (Take Care) and the patient data management system (PDMS) (Centricity Clinical Care, GE Healthcare). Patient characteristics and ICU-related data on patients treated during 2018–2019 were collected from the PDMS and the Swedish Intensive Care Registry, available through personal log-in. Collected data included age, sex, body mass index (BMI), severity of illness assessed with the Simplified Acute Physiology Score 3 (SAPS3) score at ICU admission, ICU length of stay, occurrence and duration of mechanical ventilation and mortality.

The SAPS 3 is a scoring system for severity of illness, predicting hospital mortality by scoring vital parameters, prior comorbidities (cancer, haematological cancer, chronic heart failure, cirrhosis and AIDS) and patient characteristics. A higher score indicates a greater risk of hospital mortality (Moreno et al., 2005).

Primary outcome

The primary outcome was HRQL assessed with the RAND-36 questionnaire at four to nine months after discharge from the ICU. All patients admitted to the ICU due to COVID-19 were offered hospital-based follow-up within the first year after ICU stay, timing depending on resources and patient recovery. The patients received the RAND-36 by mail, filled in the questionnaire and brought it to the follow-up appointment. Before the pandemic, ICU survivors with a minimum ICU stay of 72 hours were invited for a follow-up visit at the post-ICU clinic approximately three months after ICU

discharge. During this visit, an evaluation of their psychological, physical and cognitive status, alongside HRQL, was made. HRQL was assessed using the RAND-36 Item Health Survey. The HRQL assessment was repeated at six- and 12-month post-ICU with questionnaires sent by mail to patients. To obtain comparable groups, non-COVID-19 patients with outcome data at six months after ICU discharge and COVID-19 patients with outcome data at four to nine months after ICU discharge were included in the study.

The RAND-36 item health survey

The RAND-36 is a systematic measurement of 36 items assessing HRQL (Hays & Morales, 2001), also translated and validated in the Swedish population (Orwelius et al., 2017). It is developed from the commonly used Medical Outcomes Study Short Form-36 (SF-36). RAND-36 can be divided into eight health domains (physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, vitality, pain and general health perception), and is summarized into two component scores, the physical and mental component scores. Responses to the questionnaire are linearly transformed into scores between 0 and 100, where a higher score indicates greater HRQL. A score difference of >5 points between measurements or groups has been suggested as clinically significant (Ware, Kosinski & Dewey, 2000).

Data analysis

No formal power calculation was performed, as the sample size was determined by the number of patients available during the predefined inclusion period.Numerical data such as age, BMI, severity of injury, duration of mechanical ventilation and ICU length of stay were presented with medians and interquartile ranges (IQR), while categorical data such as sex, occurrence of mechanical ventilation and mortality were presented with frequencies and percentages. Comparisons of numerical data between patient groups were performed with the Mann-Whitney U test, and comparisons of categorical variables were made with Fisher's exact test or the Chi-square test.

RAND-36 data was analysed and summarized with means and standard deviations into the eight different domains and the physical and mental component summary scores and assumed to have a linear relation to the underlying health concept measured. (RAND Corporation, n.d.; Ware & Sherbourne, 1992). To compare HRQL between groups, linear regression models were used, also adjusting for age, sex, BMI, SAPS 3, ICU length of stay and duration of mechanical ventilation as potential confounders. All variables, except sex were treated as continuous variables in the analyses. The results from the linear regression modelling were presented as mean score differences (MSD) with 95% confidence intervals (CIs), presenting both unadjusted and adjusted results. No imputation was made for missing data.

The two-sided significance level was set at 0.05. All statistical analyses were made using R version 4.3.1 and STATA version 12.

RESULTS

Patient characteristics

Among the 257 COVID-19 patients treated in the ICU with completed follow-up, 164 patients who

reported their HRQL data between four and nine months after their ICU stay were included in the study. A total of 823 non-COVID-19 patients were treated in the ICU for a minimum of 72 hours during 2018 and 2019, of whom all 105 individuals with HRQL data six months post-ICU were included in the study. The details of patient inclusion are shown in Figure 1.

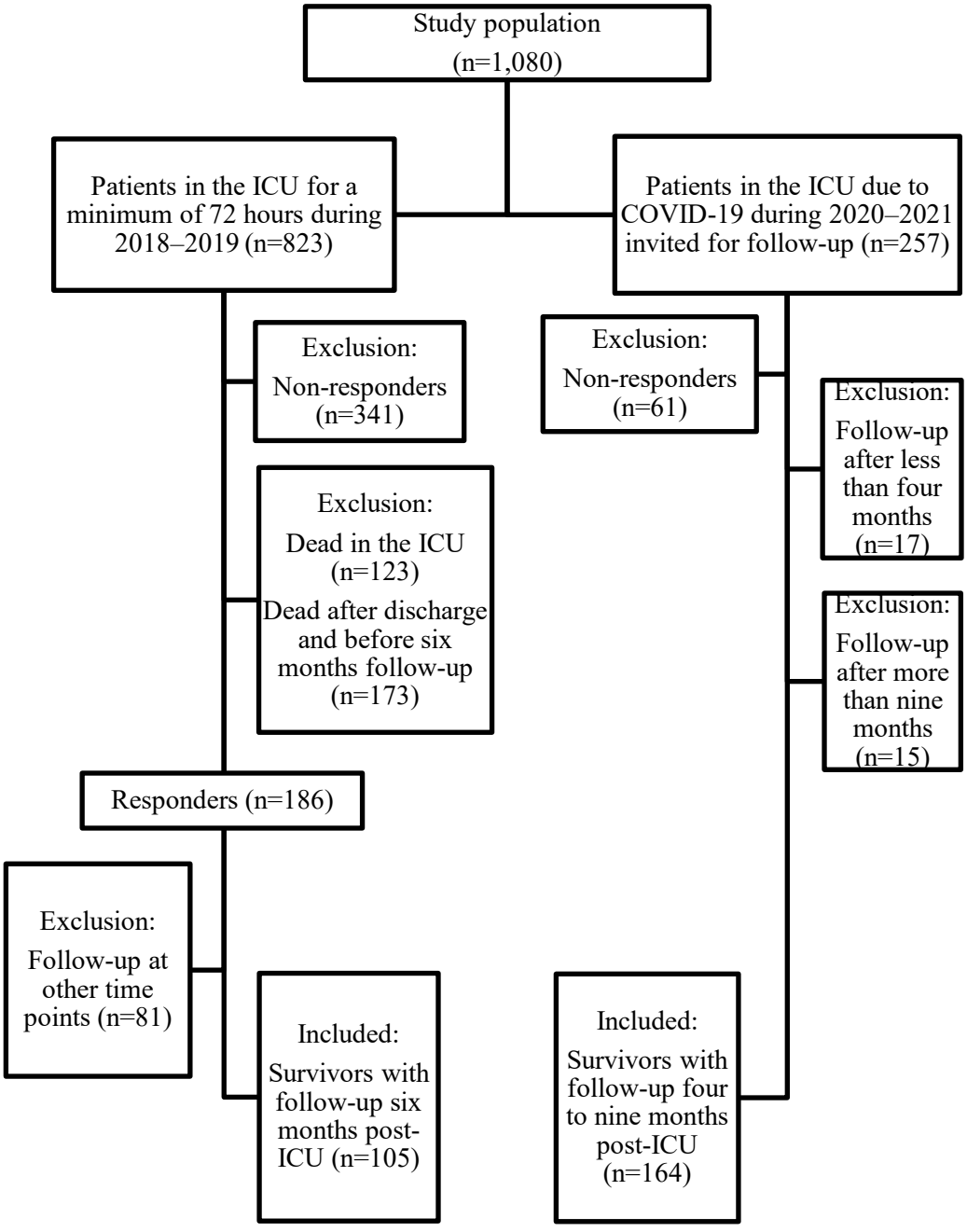

Figure 1. Flow chart of study population.

The clinical characteristics and ICU-related data of included patients are detailed in Table 1. Patients with COVID-19 were younger ($p<0.001$), with lower SAPS 3 scores ($p<0.001$), indicating less severe

illness, and a smaller proportion received mechanical ventilation (p<0.001) even though the duration of mechanical ventilation in those ventilated was longer (p<0.001). Missing data was <10% in all variables besides BMI where 15% of observations were missing. No imputation was made for BMI. For a complete description of missing data, see supplementary Table S1.

Table 1. Clinical characteristics and ICU-related data.

Patient characteristics	**Non-COVID-19 (n=105)**	**COVID-19 (n=164)**	**All included patients (n=269)**
Age (years), median (IQR)	71 (62–76)	61 (53–69)	71 (56–73)
Sex (male), n (%)	68 (65)	114 (70)	182 (68)
Length of ICU stay (days), median (IQR)	7 (4–18)	9 (5–19)	8 (5–18)
Mechanical ventilation, n (%)	79 (75)	81 (49)	160 (59)
Duration of mechanical ventilation (days)[a], median (IQR)	5 (2–13)	12 (7–24)	9 (4–19)
SAPS 3 score, median (IQR)	66 (57–75)	56 (52–60)	57 (53–66)
BMI (kg/m^2),[b] median (IQR)	27 (24–31)	28 (25–32)	28 (25–31)

[a] Including only patients receiving mechanical ventilation
[b] BMI was missing in 15% of patients, no imputation was made
IQR: Interquartile Range; ICU: Intensive Care Unit; SAPS 3: Simplified Acute Physiology Score 3; *BMI:* body mass index

Health-related quality of life

All included patients have outcome data on HRQL assessed with the RAND-36. The follow-up assessment for included COVID-19 patients was performed four to nine months after ICU discharge, median five months (IQR 5 to 6), while follow-up data for included non-COVID-19 patients was collected six months after ICU discharge. Mean RAND-36 scores in each domain and in the mental and physical component scores for both groups, and mean score differences in the unadjusted and adjusted linear regression analyses are outlined in Table 2. There were no differences in reported HRQL after ICU stay between the groups, with the exception for COVID-19 patients reporting higher HRQL in the physical function domain, mean score difference 9.5 (95% CI 2.1 to 16.9, p<0.01), compared to the non-COVID-19 group. This difference was not sustained when adjusting for the predefined confounders age, sex, BMI, SAPS 3 score, duration of mechanical ventilation and length of ICU stay. Additionally, there was a trend towards higher HRQL in the COVID-19 population in the other domains excluding vitality and bodily pain, but these differences were not statistically significant.

Table 2. Health-related quality of life for COVID-19 and non-COVID-19 survivors

RAND-36 domain	Non-COVID-19 patients (n=105)	COVID-19 patients (n=164)	Mean score difference, unadjusted analysis[a] (95% CI) p-value	Mean score difference, adjusted analysis[b] (95% CI) p-value
Physical function	53 (31.6)	63 (27.6)	9.5 (2.3 to 16.7) 0.01*	7.5 (-2.7 to 17.7) 0.15
Role physical	35 (40.4)	42 (44.8)	7.7 (-2.8 to 18.1) 0.16	10.1 (-5.8 to 26.0) 0.21
Bodily pain	64 (29.9)	65 (28.9)	0.9 (-6.4 to 8.14) 0.82	-4.8 (-15.7 to 6.1) 0.39
General health	50 (20.9)	53 (22.3)	2.5 (-2.8 to 7.9) 0.36	5.5 (-3.4 to 14.3) 0.22
Vitality	55 (23.8)	51 (24.1)	-4.8 (-10.7 to 1.1) 0.11	-0.6 (-9.3 to 8.1) 0.89
Social function	64 (28.8)	65 (28.1)	1.7 (-5.3 to 8.8) 0.63	5.3 (-4.4 to 15.0) 0.28
Role emotional	58 (43.4)	64 (41.8)	6.0 (-4.7 to 16.6) 0.27	16.9 (-1.7 to 35.4) 0.07
Mental health	70 (21.4)	71 (20.2)	0.6 (4.6 to 5.8) 0.82	4.0 (-4.3 to 12.3) 0.34
Physical component summary score	51 (25.0)	55 (25.2)	4.9 (-1.3 to 11.0) 0.12	3.8 (-4.8 to 12.5) 0.38
Mental component summary score	62 (25.1)	63 (23.7)	0.8 (-5.2 to 6.9) 0.79	6.0 (-2.9 to 14.9) 0.19

The RAND-36 domain scores are presented as means (±standard deviation) and mean score differences with 95% CIs.
CI: confidence interval
[a] Non-Covid-19 patients as reference
[b] Adjusted for age, sex, BMI, SAPS 3, duration of mechanical ventilation and length of ICU stay
*Significant p-value, analysed with the Mann-Whitney U test

DISCUSSION

In this cohort study, with the aim of assessing differences in health-related quality of life after ICU stay between COVID-19 and non-COVID-19 survivors admitted before the pandemic, no statistically significant differences between the groups could be demonstrated. In the unadjusted analysis, the COVID-19 population reported a clinically relevant and statistically significant difference, indicating better HRQL, in the physical function domain. When adjusting for potential confounders, however, no significant differences remained. This indicates that observed differences were more likely a result of variations in patient characteristics rather than actual disparities between the groups.

Previous studies comparing HRQL between older COVID-19 patients and non-COVID-19 patients before and during the pandemic, as well as between all ICU patients during the pandemic, have also indicated a lack of difference in HRQL between the groups, in line with our findings (Rousseau et al., 2023; Thiolliere et al., 2022). Another study assessing HRQL among mechanically ventilated patients without COVID-19 before the pandemic and COVID-19 patients during the pandemic did not find any differences in reported HRQL (Hodgson et al., 2022). It is also worth noting that both COVID-19 and non-COVID-19 groups exhibit reduced health-related quality of life compared to a reference population (Halvorsen et al., 2023; Cuthbertson et al., 2010; Hofhuis et al., 2021).

These results suggest that the observed reduction in HRQL may be linked to the stay in the ICU and not to the COVID-19 pandemic. As in our study, previous studies have reported differences regarding patient characteristics, with COVID-19 patients being younger and requiring extended time with mechanical ventilation compared to non-COVID-19 patients (Rousseau et al., 2023; Thiolliere et al., 2022; Palacios-Moguel et al., 2023), except for one study where included COVID-19 patients were older (Hodgson et al., 2022). It is crucial to recognize this heterogeneity regarding patient characteristics as well as comorbidities, the care received in the ICU and rehabilitation after ICU stay. These differences pose a challenge when drawing conclusions from study results, as they have the potential to influence the outcome.

Unlike other studies that consistently reported a higher proportion of COVID-19 patients requiring mechanical ventilation compared to non-COVID-19 patients (Rousseau et al., 2023; Palacios-Moguel et al., 2023), the COVID-19 patients in our study required mechanical ventilation to a lesser extent than the non-COVID-19 patients. This could be interpreted as the non-COVID-19 patients being more critically ill than the COVID-19 patients. On the other hand, the median duration of mechanical ventilation was longer in the COVID-19 group, suggesting that mechanically ventilated patients with COVID-19 experienced more severe respiratory failure. A potential explanation for the lower rate of mechanical ventilation for COVID-19 patients in our study could be the common use of non-invasive ventilation despite severe respiratory failure during the second and third waves of the pandemic.

When analysing post-ICU HRQL between the groups, it is interesting to consider the role of PICS and long-term COVID in the recovery process. One could assume that post-acute symptoms of COVID-19 virus infection (long COVID) would affect HRQL negatively, implying worse HRQL in COVID-19 patients compared to regular ICU patients. However, due to the similarity of symptoms in PICS and long COVID, there have been discussions on whether some ICU survivors with long COVID may be

experiencing PICS, rather than long COVID (Yong & Liu, 2022). In previous studies, the proportion of patients with PICS was similar, regardless of whether they survived COVID-19 or any other critical illness, which is also in line with our results of similar HRQL in both COVID-19 and non-COVID-19 groups (Rousseau et al., 2023; Hodgson et al., 2022).

During the pandemic, intensive care underwent significant changes, prompting the consideration of potential effects on HRQL. In the early phases of the pandemic, the understanding of treating COVID-19 was limited, causing concerns that COVID-19 patients might receive suboptimal care compared to patients treated before the pandemic, with known diagnoses and existing medical guidelines. As the pandemic progressed, knowledge about the COVID-19 disease increased, and intensive care practices became more standardized and normalized. Despite these original concerns, previous research has indicated that the HRQL of COVID-19 patients remained relatively constant, regardless of when they received care during the pandemic (Darlington et al., 2023).

Overall, our findings indicate that the impact of circumstances during the pandemic may have been less substantial than initially expected. The results also highlight a potential resilience in ICU care and patient recovery processes, even during crises such as the COVID-19 pandemic. This implies that identification and follow-up of post-ICU symptoms can be relevant for all ICU survivors, regardless of the initial diagnosis and the circumstances of the provided critical care.

Strengths and limitations

Our results should be interpreted considering the strengths and limitations of the study. The inclusion of a heterogeneous ICU population of adult patients of different ages in a mixed ICU environment is a notable strength, increasing the generalizability of the results. Another strength is the use of the validated and widely used RAND-36 questionnaire, with different domains aiding in evaluating specific aspects of HRQL.

However, this study also has limitations. As the sample size was determined by the number of patients followed during a predefined study period, no power calculation was performed prior to recruitment, and a larger population would have provided more robust results. Another concern is the potential for selection bias, with a lower proportion of patients among the non-COVID patients responding to the follow-up questionnaire, potentially limiting conclusions drawn about this cohort. Individuals who are unable or unwilling to answer the follow-up questionnaire due to a poor recovery or individuals who choose not to answer due to a good recovery could both be underrepresented, potentially affecting the findings. Data on comorbidities was limited to the information obtained in the SAPS 3, with scarce information on pre-ICU health. Another limitation of the study is that socioeconomic factors were not assessed, which may influence the findings and their interpretation. Additionally, the study measures HRQL only at a single time point, 4 to 9 months after ICU care. During this interval, HRQL may be influenced by various life events unrelated to prior ICU treatment or the underlying condition. This limitation suggests that changes in HRQL could arise from factors not associated with the intensive care experience.

Our study setting is intensive care at one large tertiary care hospital in Sweden during selected periods. It is essential to bear in mind that healthcare and resources varied across different regions during the pandemic. Our study population may not reflect ICU populations in other countries, and there may be differences in gender, age distribution and socioeconomic aspects compared to ICU-treated patients in other parts of the world, limiting the generalizability of our findings.

CONCLUSION

In conclusion, our study results, with no significant difference in HRQL post-ICU between COVID-19 patients and patients admitted before the pandemic, suggest that the impact of circumstances during the pandemic may have been less significant than what could have been expected. This implies that identification and follow-up of post-ICU symptoms are relevant for all ICU survivors, irrespective of the initial diagnosis.

Authors' contributions

Data collection was performed by Anni Tanskanen, Anna Schandl, Anna Milton, Pernilla Darlington and Anders Hedman. Data analysis was performed by Anna Milton and Anni Tanskanen. A first manuscript draft was written by Anni Tanskanen under supervision by Anna Milton. All authors read the manuscript and contributed to the development of the final submitted version of the manuscript.

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