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RESEARCH ARTICLE

Characteristics and definitive outcomes of COVID-19 patients admitted to a secondary hospital intensive care unit in Sweden

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Abstract

Background and Aims: Most published reports of COVID-19 Intensive Care Unit (ICU) patients are from large tertiary hospitals and often present short-term or incomplete outcome data. There are reports indicating that ICUs with fewer beds are associated with higher mortality. This study aimed to investigate the definitive outcome and patient characteristics of the complete first wave of COVID-19 patients admitted to ICU in a secondary hospital.

Methods: In this prospective observational study, all patients with respiratory failure and a positive SARS-CoV-2 test admitted to Västerås Hospital ICU between 24 March and July 22, 2020 were included. The primary outcome was defined as 90-day mortality. Secondary outcomes included ICU length of stay, hospital length of stay, number of days with invasive ventilation, need for vasopressors/inotropes, and use of renal replacement therapy.

Results: Fifty-three patients were included. Median age (range) was 59 (33-76) and 74% were men. Obesity and hypertension were the most common comorbidities and 45% of the patients were born outside Europe. Ninety-day mortality was 30%. Median ICU length of stay (interquartile range) was 14 (5-24) days and the duration of invasive mechanical ventilation 16 (12-26) days. No patients received dialysis at 90-day follow-up.

Conclusion: In this cohort of COVID-19 patients treated in a secondary hospital ICU, mortality rates were low compared to early studies from China, Italy, and the United States, but similar to other government-funded hospitals in Scandinavia. A preparatory reorganization enabled an increase in ICU capacity, hence avoiding an overwhelmed intensive care organization.

KEYWORDS

90-day follow-up, ARDS, COVID-19, critical care, ICU capacity, intensive care, long-term, mortality, outcome, SARS-CoV-2

1 | INTRODUCTION

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has put a serious strain on Intensive Care Units (ICUs) around the globe. Vast regional differences in disease burden have been reported along with variable mortality rates.[1-6] Sweden has received media attention for its pandemic strategy and demonstrated in late 2020, an eight-times higher mortality rate than the most

affected Scandinavian neighbour, Denmark.[7] Furthermore, the health care system in Sweden is divided into 21 almost autonomous regions that may display outcome differences.

To date, most published reports on outcomes from COVID-19 ICU patients have been either multicenter studies, many of which nationwide and registry-based,[8-12] or studies from large tertiary hospitals.[2,3,5] Tertiary hospitals have, compared to smaller secondary hospitals, better access to advanced care such as extracorporeal membrane oxygenation (ECMO) and, possibly, a greater capacity to expand and reorganize intensive care in terms of staff and facilities. In accordance, one recent nationwide COVID-19 study from the United States (US) indicated that ICUs with fewer beds were associated with higher mortality.[9]

Västerås Hospital provides secondary care in the region of Västmanland and has an ICU with one of the lowest ICU capacities per capita in the country.[13] Before the pandemic, Västerås Hospital provided a single ICU with eight beds, in a catchment area consisting of approximately 275 000 residents, equivalent to 2.9 ICU beds/100 000 inhabitants. The average national ratio is 5.1 ICU beds/100 000 inhabitants,[13] compared to an average of 11.5 in Europe, although there is a substantial spread.[14] This observational study aimed to describe patient characteristics and definitive outcomes from the entire cohort of patients with COVID-19 receiving intensive care in Västerås Hospital during the first phase of the pandemic.

2 | METHODS

2.1 | Study design and participants

This prospective observational cohort study was approved by the Regional Ethics Committee in Uppsala (approval number 2020-02315) with a waiver of informed consent. It was registered at ClinicalTrials.gov (NCT04382417) and conducted in accordance with the 1964 Declaration of Helsinki.

All patients with respiratory failure and a positive real-time reverse transcription polymerase chain-reaction (RT-PCR) test admitted to the ICU between 24 March and July 22, 2020 were included in the study. Patients with negative RT-PCR but with radiological or clinical suspicion of COVID-19 were excluded. The time of recruitment corresponded to the complete first wave of the pandemic in this region. The last patient with COVID-19 treated in the ICU was discharged on July 22, 2020. An individual 90-day follow-up was carried out for each patient, starting from the date of admission to the ICU. The study end point, October 20, 2020, thus represented the 90-day follow-up for the last patient admitted to the ICU during this phase.

2.2 | Setting

Västerås Hospital is a public, secondary care hospital situated approximately a one-hour drive from the capital city of Stockholm. As for all ICUs in Sweden, the care provided is entirely government-funded. Patients in need of ECMO, cardiac-, or neurosurgery are referred to tertiary hospitals in Stockholm or Uppsala.

During the first wave of the pandemic in early 2020, the viral transmission in the region exhibited an approximate 2-week delay compared to Stockholm. This enabled a substantial reorganization, to prepare for the anticipated surge of patients requiring intensive care. Elective non-malignant surgery was postponed, and overall, elective surgery capacity was reduced to 50% to enable expanded ICU cohort care. One of the post-anesthesia care units in the hospital was rearranged to create a separate enclosed ICU with 14 beds dedicated to COVID-19 patients. The general ICU capacity for non-COVID-19 patients was reduced from eight to five beds. Physicians and nurses without intensive care training from other parts of the health care system were relocated to assist in the new ICU. Anaesthetic ventilators from the operating theatre were brought in and rationing of syringe pumps became necessary. Commonly used sedatives like propofol and remifentanil were intermittently out of stock and substituted for longer-acting agents such as midazolam and morphine. Frequent prioritization of patients eligible for either continuous renal replacement therapy or hemodialysis had to be done according to availability and hemodynamic stability.

2.3 | Hospital organization

A temporary triage tent with a tailored algorithm for COVID-19 related symptoms was established in conjunction with the Emergency Department. Depending on the severity of symptoms, test results, and clinical suspicion, patients were either transferred to dedicated COVID-19 hospital wards, triage isolation, or directly to the ICU. Worsening hypoxemia [defined as peripheral oxygen saturation (SpO_2) <95% despite high flow nasal oxygen therapy (HFNO) 45 L/min with 70% fraction of inspired oxygen (FiO_2) or oxygen reservoir mask >10 L/min] and the practice of awake prone positioning on the ward prompted a clinical and individual assessment to investigate eligibility for intensive care. Thus, not all patients fulfilling the above criteria were admitted to the ICU.

2.4 | Data collection and variables

All patients fulfilling study inclusion criteria were continuously enrolled and double-checked through the Swedish Intensive Care Registry, using the code for COVID-19, U07.1, as stipulated in the International Classification of Diseases, 10th Revision. Clinical and laboratorial data were retrieved from the existing electronic medical record (Cosmic R82.05, Cambio Health Care Systems, Sweden).

Clinical data regarding patient characteristics, pre-existing comorbidities, symptom onset prior to hospitalization, medications and complications during intensive care, ventilator settings, laboratory results, 90-day mortality, and hospital length of stay were collected.

Registered comorbidities were defined as: obesity (Body Mass Index, BMI >30), hypertension (use of antihypertensive medication),

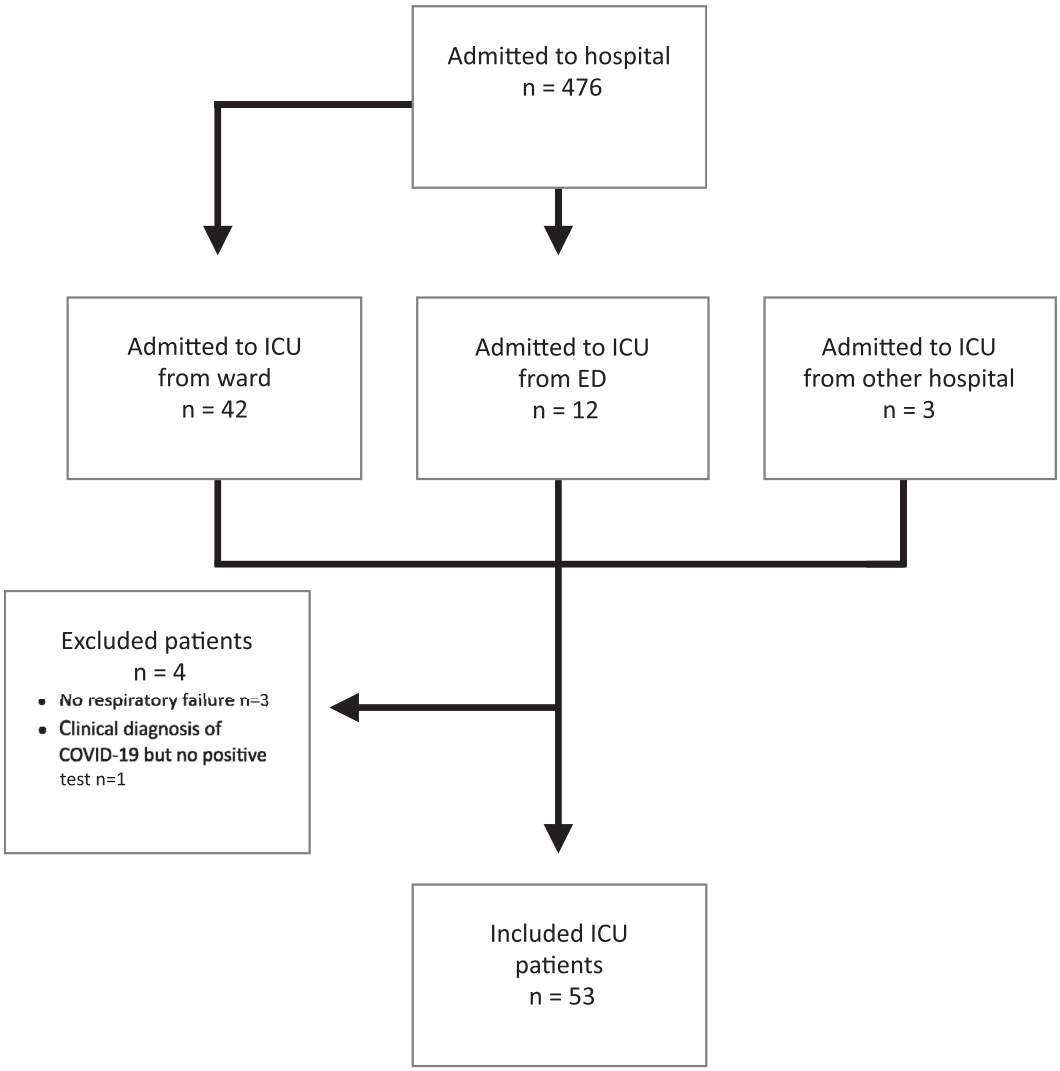

FIGURE 1 CONSORT diagram for confirmed cases of SARS-CoV-2 admitted to Västerås hospital during the study period (between 24 March and July 22, 2020). SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; ED: Emergency department; ICU: Intensive Care Unit

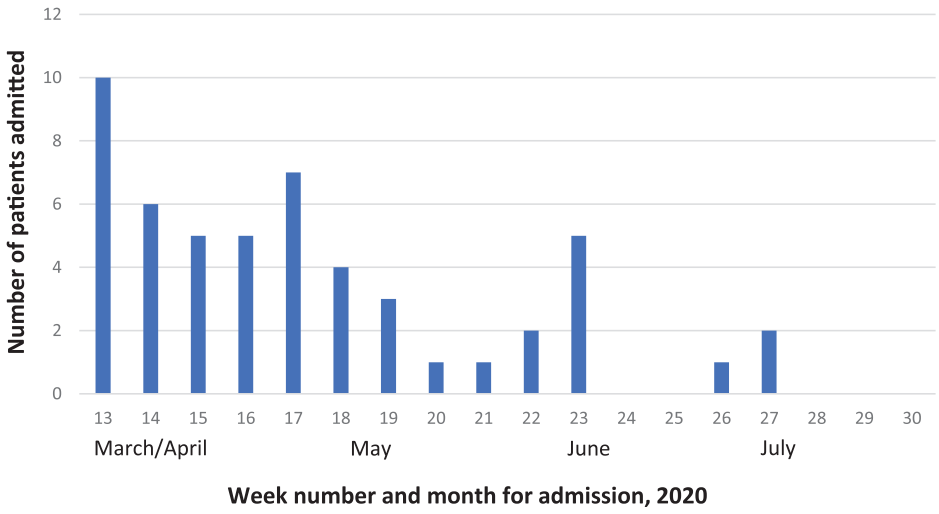

FIGURE 2 Number of patients admitted to ICU per week number and month. ICU, intensive care unit

TABLE 1 Patient characteristics

	All patients $n = 53$	Survivors $n = 37$	Non-survivors $n = 16$
Characteristics			
Age, years	59 (33-76)	54 (33-76)	63 (41-75)
<40	2	2	0
40-49	10	9	1
50-59	15	12	3
60-69	17	10	7
≥70	9	4	5
Male sex	39 (74%)	26 (70%)	13 (81%)
Place of birth			
Sweden	25 (47%)	15 (41%)	10 (63%)
Europe	4 (8%)	4 (11%)	-
Outside Europe	24 (45%)	18 (49%)	6 (38%)
Days with symptoms prior to			
Hospitalisation	9 (6-11)	9 (7-11)	8 (6–11)
ICU admission	11 (8-13)	11 (9-13)	11 (8-12)
Intubation	11 (3-25)	11 (3-19)	12 (8-25)
Prior site to ICU admission			
ED	11 (21%)	6 (16%)	5 (31%)
External ICU	3 (6%)	2 (5%)	1 (6%)
Hospital ward	39 (74%)	29 (78%)	10 (63%)
Comorbidities			
Obesity	27 (52%)	20 (54%)	7 (44%)
Hypertension	24 (45%)	17 (46%)	7 (44%)
Diabetes	13 (25%)	9 (24%)	4 (25%)
COPD or asthma	9 (17%)	5 (14%)	4 (25%)
Ischemic heart disease	2 (4%)	1 (3%)	1 (6%)
Immunocompromise	4 (8%)	2 (5%)	2 (13%)
Heart failure	-	-	-
Chronic kidney disease	-	-	-
Cancer	-	-	-
One comorbidity	15 (28%)	10 (27%)	5 (31%)
Two comorbidities	18 (34%)	14 (38%)	4 (25%)
More than two comorbidities	8 (15%)	5 (14%)	3 (19%)
No comorbidity	12 (23%)	8 (22%)	4 (25%)
Current smoker	4 (8%)	3 (8%)	1 (6%)

Note: Age data are expressed as median (range). Subsequent data are median (interquartile range) or *n* (%).
Abbreviations: COPD, Chronic obstructive pulmonary disease; ED, emergency department; ICU, intensive care unit.

diabetes mellitus (use of antidiabetic medication), chronic obstructive pulmonary disease (COPD) or asthma (use of inhalers and verified by spirometry), ischemic heart disease (history of myocardial infarction, previous coronary stenting, stable or unstable angina pectoris), immunocompromise (use of any systemic immunosuppressive medication), heart failure (ejection fraction <40% and/or New York Heart Association Classification of stage 3 or 4), chronic kidney disease (GFR ≤60 mL/min/1.73 m^2) and cancer (with ongoing active treatment).

2.5 | Outcomes

Primary outcome was defined as all-cause mortality at 90-day follow-up starting from ICU admission. Secondary outcomes included 90-day hospital discharge, patient characteristics, ICU length of stay, hospital length of stay, number of days with invasive ventilation, need for vasopressors/inotropes, and number of patients receiving renal replacement therapy (RRT). Data were supplemented with a gross functional outcome and 6-minutes walking distance (6MWD) from

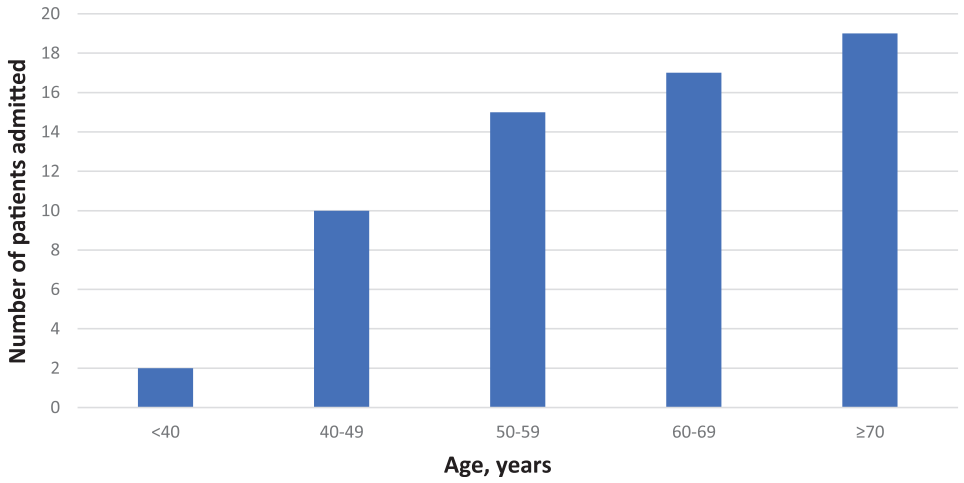

FIGURE 3 Age distribution of included patients. ICU, intensive care unit

TABLE 2 Medication and complications during ICU stay

	All patients $n = 53$	Survivors $n = 37$	Non-survivors $n = 16$
Medication			
Hydroxychloroquine	12 (23%)	9 (24%)	3 (19%)
Corticosteroids	17 (32%)	8 (22%)	9 (56%)
Dalteparin	53 (100%)	37 (100%)	16 (100%)
Heparin	15 (28%)	7 (19%)	8 (50%)
Systemic antifungal treatment	19 (36%)	8 (22%)	11 (69%)
Antibiotics			
One antibiotic	16 (30%)	15 (41%)	1 (6%)
Two antibiotics	12 (23%)	10 (27%)	2 (13%)
More than two antibiotics	23 (43%)	11 (30%)	12 (75%)
No antibiotic	2 (4%)	1 (3%)	1 (6%)
Complications			
Pulmonary embolism[a]	6 (11%)	4 (11%)	2 (13%)
Deep vein thrombosis	1 (2%)	-	1 (6%)
Cerebrovascular insult	1 (2%)	1 (3%)	-
Intestinal ischemia	1 (2%)	-	1 (6%)
Myocardial infarction	1 (2%)	-	1 (6%)
Right ventricular failure[b]	11 (21%)	7 (19%)	4 (25%)
Bleeding	5 (9%)	3 (8%)	2 (13%)
Brain haemorrhage	3 (6%)	2 (5%)	1 (6%)
Superimposed bacterial or fungal infection	18 (34%)	12 (32%)	6 (38%)
Unintentional decannulation and/or extubation	2 (4%)	1 (3%)	1 (6%)

Note: Data are *n* (%).
[a]Verified by computed tomography.
[b]Verified by echocardiography.

surviving patients treated in the ICU more than 4 days, and who accepted an invitation to the post-ICU reception. As a further secondary outcome, one-year mortality was also added.

2.6 | Statistical methods

Mere descriptive statistics were used due to the size of the study population. Data are described using median (range), median (interquartile range), and count (percentage).

3 | RESULTS

Fifty-three patients with COVID-19 admitted to the ICU between 24 March and July 22, 2020 were included in this study. Four patients were excluded, as outlined in the CONSORT diagram (Figure 1).

The peak of ICU admissions during the first wave of the pandemic in this region was during the last week of March, with 10 patients admitted (Figure 2). The maximum number of patients receiving intensive care for COVID-19 at the same time was 13.

TABLE 3 Organ support

	All patients $n = 53$	Survivors $n = 37$	Non-survivors $n = 16$
Vasopressor	40 (74%)	24 (65%)	16 (100%)
RRT	15 (28%)	8 (22%)	7 (44%)
Ventilation management			
HFNO	37 (70%)	26 (70%)	11 (69%)
NIPPV	20 (38%)	15 (41%)	5 (31%)
Invasive ventilation	40 (75%)	24 (65%)	16 (100%)

Note: Data are *n* (%).
Abbreviations: HFNO, high flow nasal oxygen; NIPPV, non-invasive positive pressure ventilation; RRT, renal replacement therapy.

TABLE 4 Invasive ventilation management

	All patients on invasive ventilation $n = 40$	Survivor $n = 24$	Non-survivor $n = 16$
Days with symptoms prior to intubation	11 (9-14)	11 (9–13)	12 (9-16)
Days with invasive ventilation			
ARDS class	16 (12–26)	16 (11-29)	15 (12-23)
Mild	1 (2,5%)	1 (4%)	-
Moderate	9 (23%)	7 (29%)	2 (13%)
Severe	30 (75%)	16 (67%)	14 (88%)
Prone positioning	28 (70%)	14 (58%)	14 (88%)
Neuromuscular blockade	26 (65%)	13 (54%)	13 (81%)
Tracheotomy	19 (48%)	12 (50%)	7 (44%)

Note: Data are median (IQR) or *n* (%). End of invasive ventilation was defined as ≥24 hours without the use of a respirator.
Abbreviation: ARDS, Acute respiratory distress syndrome.

TABLE 5 Follow-up data

	All patients $n = 53$	Survivors $n = 37$	Non-survivors $n = 16$
30-day mortality	12 (23%)	-	-
90-day mortality	16 (30%)	-	-
1-year mortality	16 (30%)	-	-
ICU length of stay	14 (5–24)	11 (4-21)	17 (13-30)
Two weeks or more in the ICU	28 (53%)	16 (43%)	12 (75%)
Discharged from the ICU	37 (70%)	36 (100%)	1 (6%)
Hospital length of stay	20 (15-37)	21 (12-45)	19 (16-32)
Discharged from hospital	33 (62%)	33 (89%)	-
Remaining need of dialysis	-	-	-

Note: Data are median (IQR) or *n* (%). ICU, intensive care unit. Four patients remained in hospital at 90-day follow-up.

In the total cohort, the median age (range) was 59 (33-76) and most patients were men, 39/53 (74%) (Table 1). Age distribution is outlined in Figure 3. The most common comorbidity was obesity, followed by hypertension (Table 1). Twenty-eight patients (55%) were born outside Sweden, mostly outside Europe (Table 1). The most common countries of birth, after Sweden, were Iraq, Somalia, Iran, and Syria, in descending order.

Twelve patients (23%) received off-label treatment with hydroxychloroquine (Table 2), before the Swedish Medical Products Agency discouraged treatment on April 2, 2020, awaiting results from clinical studies.[15] Seventeen patients (32%) were for various reasons treated with corticosteroids, most commonly because of septic shock (Table 2). The last two patients to be admitted received corticosteroids according to The RECOVERY Collaborative Group study.[16] All patients in the ICU had standard pharmacological thrombosis prophylaxis (Dalteparin) according to weight, up until May 8, 2020, when the Swedish guidelines regarding thromboprofylaxis in COVID-19 were released following scientific report showing a high incidence of thrombotic events associated with COVID-19.[17]

Forty patients (75%) received invasive mechanical ventilation, and thirty of these were considered having severe Acute Respiratory

Distress syndrome (ARDS), according to the Berlin criteria (Table 3).[18] Neuromuscular blockade and prone positioning were used in 70 and 65%, respectively, of the patients receiving invasive mechanical ventilation (Table 4). A continuous dialogue with ECMO-centers at tertiary hospitals was held for all patients with refractory hypoxemia but none of these were deemed eligible after assessment.

A complete 90-day follow-up of the entire cohort was carried out at the study end point, October 20, 2020. Sixteen patients (30%) had died, of whom 15 in the ICU, most often after a decision to discontinue life-sustaining support (Table 5). The mortality rate for patients receiving mechanical ventilation was 16/40 (40%). All patients who had received RRT during their ICU stay and were alive at study end point exhibited reversible renal failure without the need for further dialysis.

Among the entire cohort, 27/53 patients were eligible for a return visit at the post-ICU reception (10 patients had not been treated for more than 4 days in the ICU and 16 were deceased). Unfortunately, 11/27 did not respond when contacted by phone and mail. For the remaining 16 patients, medical consultations could be made with a median (range) follow-up time of 33 (22-60) weeks after ICU admission. Of these 16 patients, 5 declared by phone that they were not interested or dared visiting the hospital at this stage of the pandemic. Three experienced a full physical and mental recovery and 2 reported nearly full physical recovery. One of these patients also suffered from symptoms associated with posttraumatic stress syndrome. The remaining 11 patients paid a physical visit at the post-ICU reception and 6 of them had a reduced 6MWD, with values below 571 m.[19] At the 1-year follow-up, no additional deaths had occurred compared to the follow-up at 90 days.

Documentation was inadequately registered for one patient regarding BMI, three patients regarding smoking habits, and one patient regarding the day of symptom onset. Remaining data were complete for the entire cohort.

4 | DISCUSSION

This prospective observational cohort study describes the definitive outcome of the complete first wave of patients treated in the ICU of a secondary hospital with a pre-pandemic low ICU capacity.

The mortality rate in this cohort (30%) was lower than rates reported in early studies from China, Italy, and the United States,[2,3,20] but comparable with data from similar government-funded health care systems in Sweden and Denmark.[8,10] However, comparing mortality data between different ICUs is difficult. Several factors are at play, most important criteria for ICU admission and how intensive care is defined.[14,21] In general, mortality rates for COVID-19 ICU patients have decreased since the beginning of the pandemic,[1] possibly due to increased knowledge about the disease and the introduction of new or adjusted therapies, for example intensified anticoagulant therapy[22] and widespread treatment with dexamethasone.[16] The results from this study reflect the early phase of the pandemic, since only the last two patients to be admitted received dexamethasone in accordance with The RECOVERY Collaborative Group study.[16]

One factor that has been suggested to affect mortality is ICU capacity.[9] Gupta et al reported a higher risk of death for COVID-19 patients admitted to US hospitals with <50 ICU beds compared to hospitals with ≥100 ICU beds. A direct comparison with the Swedish health care system is difficult. However, it is presumable that larger hospitals are better equipped to reorganize and expand intensive care, not least regarding the ability to increase staffing. In Europe, ICU capacity ranges from 4.2 to 29.2 beds per 100 000 inhabitants, with an average of 11.5 beds per 100 000 inhabitants.[14,21] Heterogeneous definitions, especially regarding the distinction between intermediate and intensive care, are probably a major factor explaining the wide range.[14,21] Nevertheless, ICU capacity certainly differs between countries and regions, and the pre-pandemic capacity of 2.9 ICU beds per 100 000 inhabitants in the studied region was indeed low. Although the sample size was small, the mortality data in this study do not support that low ICU capacity correlates with higher mortality in critically ill COVID-19 patients. However, it is likely that the health care system benefitted from the 2-week delay in the spread of the virus, compared to nearby regions. This enabled a substantial reorganization before the first patient was admitted to intensive care. This contributed to the fact that ICU capacity was not exceeded at any time during the study period and perhaps calls for a more dynamic definition of ICU capacity.

Similar to most ICU studies, the majority of the patients in the study were men above middle age (Table 1).[2,3,10,11] Obesity and hypertension were the predominant comorbidities. Notably, a considerable proportion of patients (23%) had no known systemic disease prior to ICU admission. Moreover, there were no patients with preexisting heart failure, active cancer, or chronic kidney disease in the data, which might reflect pre-ICU decisions on limiting life support in some patients. However, data on COVID-19 patients treated in the hospital outside ICU were not collected in this study. Most of the included patients (57%) developed severe ARDS. RRT for acute kidney injury was used in 28% of the cases. Interestingly, none of the patients who received dialysis during their ICU stay and were still alive at 90-day follow-up had a residual need, suggesting a totally reversible acute kidney injury among survivors.

Several previous studies have shown a higher incidence of severe COVID-19 in need of intensive care among patients of some ethnic groups.[9,23,24] This study has a similar finding, with a disproportionate percentage of patients being born outside Sweden. Of the ICU cohort, 55% of the patients, compared to 23% of the corresponding age-group in the region of Västmanland, were born abroad.[25] Socioeconomic factors have been suggested to be important but do not fully explain the association between ethnicity and severity of COVID-19.[26]

The study has important limitations. The sample was small and did not allow statistical analyses to be performed of, for example, factors associated with poor outcome. The small sample size and the regional nature of the data naturally enable limited generalization. The strength of this study is its prospective nature with the inclusion of every available patient and complete 90-day follow-up for the entire cohort. The record of patient characteristics had almost no missing data. To increase our understanding of COVID-19 and difficulties in delivering intensive care during a pandemic, long-term outcomes are

needed, and national and regional differences should be considered. Therefore, reports from secondary hospitals constitute a complement to studies from large, tertiary hospitals.

5 | CONCLUSION

We conclude that mortality rates from this secondary hospital ICU were low compared to early studies in China, Italy, and the United States, but comparable to other government-funded hospitals in Scandinavia. With timely reorganization, the number of ICU beds, and thus surge capacity, can increase substantially also in smaller hospitals.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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I, the corresponding author, confirm that I had full access to all of the data in the study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

I as corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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