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ORIGINAL ARTICLE

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Characteristics, management and survival of ICU patients with coronavirus disease-19 in Norway, March-June 2020. A prospective observational study

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Background: Norwegian hospitals have operated within capacity during the COVID-19 pandemic. We present patient and management characteristics, and outcomes for the entire cohort of adult (>18 years) COVID-19 patients admitted to Norwegian intensive care units (ICU) from 10 March to 19 June 2020.

Methods: Data were collected from The Norwegian intensive care and pandemic registry (NIPaR). Demographics, co-morbidities, management characteristics and outcomes are described. ICU length of stay (LOS) was analysed with linear regression, and associations between risk factors and mortality were quantified using Cox regression.

Results: In total, 217 patients were included. The male to female ratio was 3:1 and the median age was 63 years. A majority (70%) had one or more co-morbidities, most frequently cardiovascular disease (39%), chronic lung disease (22%), diabetes mellitus (20%), and obesity (17%). Most patients were admitted for acute hypoxaemic respiratory failure (AHRF) (91%) and invasive mechanical ventilation (MV) was used in 86%, prone ventilation in 38% and 25% of patients received a tracheostomy. Vasoactive drugs were used in 79% and renal replacement therapy in 15%. Median ICU LOS and time of MV was 14.0 and 12.0 days. At end of follow-up 45 patients (21%) were dead. Age, co-morbidities and severity of illness at admission were predictive of death. Severity of AHRF and male gender were associated with LOS.

Conclusions: In this national cohort of COVID-19 patients, mortality was low and attributable to known risk factors. Importantly, prolonged length-of-stay must be taken into account when planning for resource allocation for any next surge.

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1 | INTRODUCTION

Critically ill patients infected with the SARS-CoV-2 virus (COVID-19 patients) typically present with acute hypoxaemic respiratory failure (AHRF) due to viral pneumonia. This may progress to acute respiratory distress syndrome (ARDS), a common but underrecognized cause of admission to the intensive care unit (ICU) that is associated with high mortality rates and significant morbidity in survivors.[1,2] Such patients are managed in the ICU with generic measures, including invasive mechanical ventilation (MV), in accordance with evidence-based clinical practice guidelines.[3-6]

Mortality rates in ARDS of mixed aetiologies depend on patients' co-morbidities and age, severity of hypoxaemia and co-existing organ failures.[7] In the "large observational study to understand the global impact of severe acute respiratory failure" (LUNG SAFE), overall mortality for patients with ARDS was 40%.[8] The findings have pointed to a need for improved recognition of ARDS at an early stage, strict adherence to evidence-based strategies and attention to modifiable risk factors.[7] Moreover, there is a geo-economic gradient in mortality from high-income regions to low- and middle-income regions.[9]

Early reports of the management of critically ill COVID-19 patients were described in the context of health care systems that were initially overwhelmed by large numbers of patients, often exceeding the surge capacity many hospitals had planned for in the event of a pandemic.[10,11] Reported mortality rates for MV patients with COVID-19 have been high, ranging from 61.5% (China),[12] 53.4% (Italy),[13] 50% (Seattle),[14] 49.4% (UK),[15] 43.6% (New York).[16] This contrasts with outcome data for critically ill patients with non-COVID-19 viral pneumonia, eg, influenza, where mortality has been found to be considerably lower.[15]

More recently, data have emerged from healthcare systems where hospital capacity has not been strained, allowing intensive care units to provide care in accordance with established clinical practice. Although case-mix may differ, evidence is emerging that mortality in the critically ill may be lower under such circumstances.[17-20]

The first Norwegian to test positive for SARS-CoV-2 was identified 21 February 2020. This patient was probably infected in China.[21] Following this, a surge of patients (mostly vacationers returning from Northern Italy and Austria) initiated track-and-trace activities and use of quarantine. When routes of transmission could no longer be identified, Norwegian authorities initiated a society-wide lockdown beginning 12 March, including border closures, travel restrictions for health care personnel, closure of universities, schools and kindergartens. The public was barred from participation in nonessential activities (meetings, restaurants and pubs, sports) and the authorities encouraged working from home for whomever this was an option.[22] After a slow lifting of restrictions beginning 27 April, only minor local outbreaks followed until a limited "second wave" occurred in the autumn months of 2020.

Norwegian authorities organised several webinars early March, addressing the management and care for COVID-19 patients, urging preparedness in all hospitals for a surge of patients with AHRF, and stressing the importance of evidence based supportive care, including MV.[3] Hospitals were also warned that in a scenario of strained ICU-capacity, most units must be prepared to manage such patients without referral to university clinics. Use of corticosteroids and experimental therapies, including anti-virals, outside of clinical trials was actively discouraged.

In this paper we describe characteristics and management of the first wave of critically ill COVID-19 patients admitted to ICUs in Norway (March 10-June 19) and investigate factors associated with survival and length-of-stay in the ICU.

Editorial Comment

This report present a comprehensive and complete national dataset that includes all COVID-19 patients admitted to Norwegian ICUs. It describes a cross-section of both patients and their management in Norwegian ICUs during the first phase of the pandemic.

2 | METHODS

2.1 | Participants

We included all adult patients (>18 years) who were admitted to a Norwegian ICU with a diagnosis of COVID-19, between 10 March 2020 and 19 June 2020.

2.2 | Ethics

This study was approved by the South-East Norway Regional Committee for Medical and Health Research Ethics (reference no. 135310), with a waiver for informed consent. This study was registered at ClinicalTrials.gov (NCT04601090).

2.3 | Organisation and data collection

The present study is a collaboration between Oslo University Hospital and the Norwegian Intensive Care and Pandemic Registry (NIPaR), a national registry established in 1998. Since 2011, NIPaR collects individual data from all ICU-admissions in Norway, recorded securely via a web-based platform. The ordinary dataset includes patient demographics, acute physiology scores at admission, nursing workload, select treatment measures, complications and mortality. Reports with aggregate data are regularly published online and are freely available, as are detailed descriptions of variables.[23,24] From the start of the present pandemic, select co-morbidities and entries for the type and duration of ventilatory support and extracorporeal membrane oxygenation (ECMO) were

added. By late March 2020, Norwegian authorities requested that the registry be further expanded to collect national data from any patient admitted to hospital with a positive test for SARS-CoV-2. This dataset for pandemic patients includes demographics, co-morbidities, findings at the day of admission, antibiotics and classification of organ system dysfunction. Use of experimental drugs was not recorded. Detailed information regarding the variables is freely available online.[23,25] Data from the intensive care registry and the pandemic dataset was used to conduct this observational study of short-term outcomes of COVID-19 patients admitted to Norwegian ICUs (this paper).

We have also collected follow-up data corresponding to a 'core outcome measurement set' developed through an international Delphi-process for ICU patients with acute respiratory failure.[26,27] This will address the physical, psychological and cognitive health related challenges occurring after ICU treatment commonly described as "post-ICU syndrome".[28,29]

2.4 | Definitions

The primary cause for ICU-admission and the identification of ARDS in individual patients, were provided at clinicians' discretion. We did not have access to chest x-ray data or ventilator settings except for the ratio of arterial oxygen partial pressure to fractional inspired oxygen (pf-ratio) at the day of admission. For statistical analysis, we therefore classified patients according to the severity of *acute hypoxaemic respiratory failure* (AHRF) defined as either 'no invasive ventilation' or, in invasively ventilated patients as 'mild' (pf-ratio > 26.6 kPa), 'moderate' (pf-ratio > 13.3 kPa and ≤26.6 kPa) or 'severe' (pf-ratio ≤ 13.3 kPa) depending on the pf-ratio, on the first day of admission.

2.5 | Statistical analyses

Data are presented as descriptive statistics and we used time-to-event techniques to analyze survival after ICU admission. Categorical variables are reported as frequencies (percentages) and continuous variables as medians (with interquartile ranges [IQRs]) or means (with SDs).

Vital status was determined for all patients from the National Population Registry as of June 27, 2020. Kaplan-Meier survival estimates and Cox proportional hazards models were used to assess association between patient characteristics and mortality. ICU mortality rates were calculated by patient status at ICU discharge.

Days from ICU admission to death (event) or June 27, 2020 (censoring), constituted the time of analysis. At the time of censoring, all patients in this dataset were either discharged from, or dead in the ICU. For patients readmitted to the ICU after discharge, the first ICU admission was considered in the analysis. We did not include patient management data in multivariable analysis due to the risk of time-dependent bias (immortal time bias) and lack of statistical power to model this with sufficient precision. ICU LOS was log transformed and analysed with multiple linear regression using demographic data, co-morbidities and severity of illness measures as independent variables. All tests were two-sided and P-values < 0.05 were considered statistically significant. As this study was exploratory, no correction for multiple testing was done.

Stata/SE ver 15.1, StataCorp, College Station, TX, USA was used for analysis.

3 | RESULTS

3.1 | Patients

Patients' baseline characteristics are presented in Table 1 (see also Appendix Table A1). Critically ill patients were predominantly male, with a median age of 63 years, and most with one or more co-morbidities involving vital organ systems; cardiovascular disorders, lung- and kidney disease, as well as diabetes and obesity. However, in almost one-third of patients no co-morbid disease was registered by clinicians and one-fifth of patients were less than fifty years old. The cause of ICU-admission (as per clinicians' assessment) was in most cases acute respiratory failure (91.2%) (Table 1). On the first day of admission 161 patients (74.2%) required MV, with predominantly moderate or severe hypoxemic respiratory failure according to the ratio of arterial oxygen partial pressure to fractional inspired oxygen (pf-ratio) (Table 1). Thirty-four patients (15.7%) did not require MV during the first day in the ICU. We could not account for the ventilation needs on the day of admission for 22 patients. Forty-three patients (19.8%) had elevated s-urea and systolic blood pressure was lower than 100 mm Hg in 112 patients (51.6%) on the first day of admission. Respiratory failure was categorized as ARDS by clinicians in 91 patients (41.9%). Median SAPS II-score was 33.

A majority of patients were admitted between 10 March and 1 May (Figure 1) and 159 (73.3%) were admitted to hospitals in South-East Norway (capital-region) (Appendix Table A2).

3.2 | Management

Median LOS in the ICU was 14.0 days (range 0.7-69.0 days) (Table 2). One-hundred and eighty-seven patients (86.2%) were managed with MV for a median of 12.0 days and 84 patients (38.7%) were managed with non-invasive ventilation for a median of 0.7 days. Eighty-three patients (38.2%) were managed in the prone position for a median of 5 days. We have no record of prone positioning in non-MV patients. Vaso-active agents were used in a majority of patients. Thirty-two patients (14.7%) received renal replacement therapy (RRT). Tracheotomy was performed in 54 patients (24.9%). Median LOS and time on MV were 31.5 and 26.3 days, respectively, for tracheotomized patients (Appendix Table A4). Other adjuncts (ECMO, nitric oxide) were used sparingly and additional data on ventilator management was not collected.

TABLE 1 Patient characteristics

Variable	No. of patients (N = 217)	
Male (n, %)	162	74.7
Female (n, %)	55	25.3
Age (median, IQR)	63.0	54.2, 72.2
25-49 (n, %)	36	16.6
50-64 (n, %)	86	39.6
65-79 (n, %)	80	36.9
≥80 (n, %)	15	6.9
Co-morbidities and risk factors		
Any risk factor / co-morbidity (n, %)	152	70.0
Number of co-morbidities		
0 (n, %)	65	30.0
1 (n, %)	74	34.1
2 (n, %)	46	21.2
3 (n, %)	25	11.5
>3 (n, %)	7	3.2
Cardiovascular disease (incl. Hypertension) (n, %)	84	38.7
Diabetes mellitus (n, %)	43	19.8
Obesity (BMI > 30) (n, %)	38	17.5
Asthma (n, %)	32	14.8
Chronic lung disease (n, %)	18	8.3
Chronic kidney disease (n, %)	18	8.5
Impaired immune system including HIV (n, %)	18	8.1
Cancer (n, %)	8	3.7
Neurologic or neuromuscular disease (n, %)	7	3.2
Active smoker (n, %)	4	1.8
Liver disease (n, %)	1	0.5
Pregnancy (n, %)	0	0.0
No co-morbidity/risk factor (n, %)	65	30.0
Cause for ICU admission		
Respiratory (n, %)	198	91.2
Circulatory (n, %)	4	1.8
Gastroenterological (n, %)	1	0.5
Neurological (n, %)	1	0.5
Sepsis (n, %)	5	2.3
Metabolic (n, %)	1	0.5
Renal (n, %)	1	0.5
Other (n, %)	6	2.7
Illness severity at admission		
Systolic blood pressure		
<70 mm Hg (n, %)	13	6.0
70-99 mm Hg (n, %)	99	45.6
100-199 mm Hg (n, %)	97	44.7
≥200 mm Hg (n, %)	8	3.7
Acute hypoxaemic respiratory failure[b]		
Not mechanically ventilated (n, %)	34	15.7
Mild hypoxaemia[a] (n, %)	17	7.8
Moderate hypoxaemia[a] (n, %)	104	47.9
Severe hypoxaemia[a] (n, %)	40	18.4
Kidney injury[c]		
S-UREA < 10 mmol/L (n, %)	173	79.7
S-UREA 10-29.9 mmol/L (n, %)	39	18.0
S-UREA ≥ 30.00 mmol/L (n, %)	4	1.8
SAPS II-score (n = 217) (median, IQR)	*33*	*26, 41*
Clinical Frailty Scale (n = 129) (median, IQR)	*2*	*2, 3*

[a]Mild = pf-ratio > 26.6 kPa (>200 mm Hg); moderate = pf-rato > 13.3 kPa and ≤ 26.6 kPa (>100 mm Hg and ≤ 200 mm Hg); severe = pf-ratio ≤ 13.3 kPa (≤100 mm Hg).

[b]Missing: 22 pts.

[c]Missing: 1 pt.

3.3 | Outcomes

Patients were followed for a median of 89 days after ICU-admission. In total, 177 patients (81.6%) were alive at discharge from the ICU and forty patients (18.4%) died in the ICU. At the end of follow-up forty-five patients (20.7%) were dead with a median ICU LOS of 12.1 days and no patient remained in the ICU (Table 3).

Mortality rates varied depending on patient demographics and co-morbidities, management characteristics and severity of illness at admission (Table 3 and Figure 2). There were marked differences in mortality in elderly vs younger patients and mortality was higher in patients with co-morbidities. We performed several multivariable analyses to assess the impact of individual patient and disease characteristics on outcomes (Appendix Table A3). In a simplified model, we included age, the most frequently reported co-morbidities as well as co-morbidities that were significantly associated with mortality at univariate analysis. Age ≥ 65 years (hazard ratio [HR] 3.01), diabetes (HR 2.41) and chronic kidney disease (HR 2.89) were strongly associated with higher mortality (Table 4A).

Severity of illness at admission and management characteristics were also associated with different mortality rates; Patients presenting with severe acute respiratory failure, signs of kidney injury or circulatory failure, all had higher mortality (Table 3). In multivariable analysis, signs of kidney injury at admission (elevated s-urea) were independently and statistically significantly associated with death (HR 3.89) (Table 4b). The median SAPS II score was 33 and

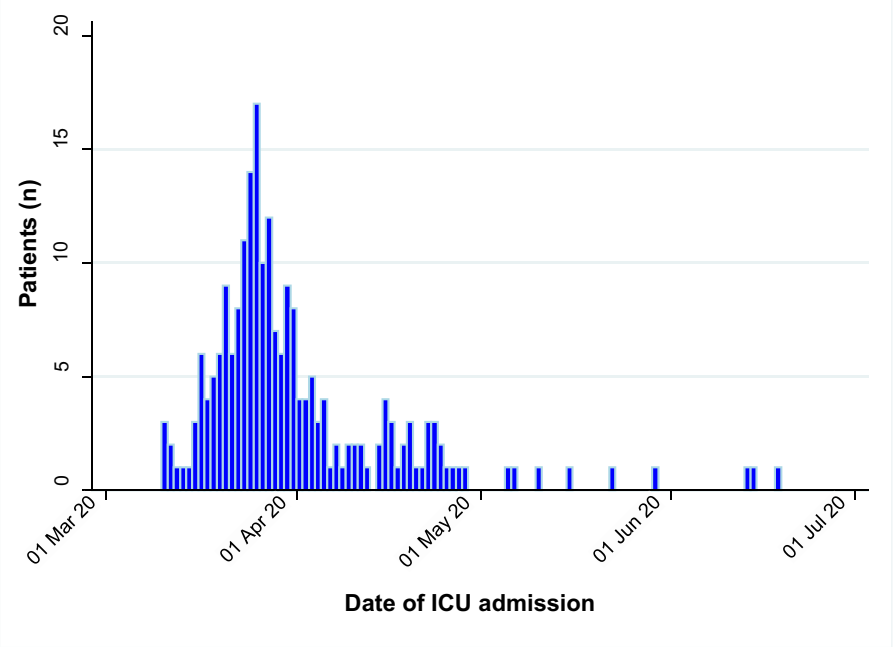

FIGURE 1 ICU admissions. Admissions (n) of COVID-19 patients are depicted by date of admission to an ICU

TABLE 2 Clinical management

	Median, IQR	n (%)
ICU-LOS (days)	14.0 (6.9, 23.0)	217 (100)
MV (days)	12.0 (6.7, 20.4)	187 (86.2)
MV in prone position (days)	5 (2.0, 8.0)	83 (38.2)
Non-invasive ventilation (days)	0.7 (0.2, 1.6)	84 (38.7)
Tracheostomy		
ICU LOS (days)	31.5 (24.1, 45.2)	54 (24.9)
Mechanical ventilation (days)	26.3 (19.8, 38.3)	54 (24.9)
ECMO (days)[a]	*(8.7, 26.3)*[a]	2 (0.9)
Nitric oxide		1(0.5%)
RRT (days)	9 (5.0, 15.0)	32 (14.7)
IHD (days)	6 (2.0, 7.0)	12 (5.5)
CRRT (days)	8.5 (5.0, 13.5)	28 (12.9)
Vaso-active drugs	-	171 (78.8)
NEMS-score (median, IQR)	513 (227, 784)	213 (98.2)

Abbreviations: ICU LOS, intensive care length-of-stay; MV, mechanical ventilation; ECMO, extracorporeal membrane oxygenation; RRT, renal replacement therapy; IHD, intermittent haemodialysis; CRRT, continuous renal replacement therapy; NEMS, nine equivalents of nursing manpower score.

[a]Range.

was a prognostic factor for death in ICU with moderate accuracy (area under the receiver operating characteristic (ROC) curve = 0.71, 95% CI [0.62-0.79]) (Appendix Figure A1L).

Mortality was higher in patients requiring organ support (mechanical ventilation, renal replacement therapy or vasoactive infusion) at any point during their stay in the ICU (Table 3). Notably, patients requiring renal replacement therapy had markedly higher mortality (53.1%) than patients who were managed without. Clinicians' identification of ARDS in these patients was of little consequence for mortality but was associated with prolonged ICU LOS (Appendix Figure A1H, Table A5).

3.4 | Resource utilisation

Mean ICU LOS and days of MV were 17.4 and 15.2, respectively (Table 5). This amounts to a total of 3771.8 days in ICU and 2840.9 days on MV (75.3% of ICU days). In contrast, non-invasive ventilation was used for only 103.6 days (2.7% of ICU-days) and renal replacement therapy for 335 days (8.9% of ICU-days). The mean "Nine equivalents of nursing manpower use score" (NEMS) per patient was 602.2. (34.6 per day in ICU). Male gender, severity of respiratory failure at admission and patients' respiratory failure classified as ARDS were all statistically significantly associated with LOS (Figure 3 and Appendix Table A5).

4 | DISCUSSION

In Norway, early public health measures resulted in a low burden of disease from COVID-19 during spring 2020.[30] As a consequence, the number of critically ill COVID-19 patients has been low and Norwegian hospitals have with few exceptions been able to remain operative within capacity, allowing management of critically

TABLE 3 Outcomes-Mortality by patient characteristics

	Discharged alive (ICU)			Death in ICU		Death at follow-up		Univariate analysis			
	N	n	%	n	%	n	%	HR	95% CI		*P*
All patients	217	177	81.6	40	18.4	45	20.7				
Gender											
Female (ref)	55	42	76.4	13	23.6	14	31.1	1.00			
Male	162	135	83.3	27	16.7	31	68.9	0.68	0.36	1.29	.24
Age											
25-49 (ref)	36	31	86.1	5	13.9	5	13.9	1.00	-	-	-
50-64	86	78	90.7	8	9.3	9	10.8	0.70	0.23	2.14	.53
65-79	80	61	76.3	19	23.8	22	27.5	2.33	0.88	6.16	.09
80+	15	7	46.7	8	53.3	9	60.0	6.36	2.13	19.03	**< .01**
Co-morbidity											
Any co-morbidity	152	118	77.6	34	22.4	39	25.7	3.04	1.29	7.20	**.01**
Heart Disease	84	63	75.0	21	25.0	25	29.8	2.10	1.16	3.79	**.02**
Any chronic lung disease[a]	47	36	76.6	11	23.4	11	23.4	1.25	0.63	2.48	.52
Diabetes	43	29	67.4	14	32.6	16	37.2	2.77	1.50	5.13	**< .01**
BMI > 30	38	31	81.6	7	18.4	7	18.4	0.77	0.32	1.92	.55
Asthma	32	25	78.1	7	21.9	7	21.9	1.10	0.49	2.46	.83
Immunodeficient	18	14	77.8	4	22.2	5	22.7	1.48	0.59	3.77	.41
CKD	18	10	55.6	8	44.4	9	50.0	3.71	1.78	7.72	**< .01**
Chronic lung disease	18	12	66.7	6	33.3	6	33.3	2.02	0.85	4.77	.11
Cancer	8	8	100.0	0	0.0	1	12.5	0.59	0.08	4.30	.60
Neurological	7	5	71.4	2	28.6	2	28.6	0.82	0.11	5.95	.84
Current Smoker	4	2	50.0	2	50.0	2	50.0	2.72	0.66	11.25	.17
Liver Disease	1	1	100.0	0	0.0	0	0.0	(omitted)			
Pregnant	0	0	-	0	-	0	-	(omitted)			
Severity at admission											
SAPS II score	217	177	81.6	40	18.4	45	20.7	1.09	1.06	1.12	**< .01**
Severity of AHRF											
no MV (ref)	34	32	94.1	2	5.9	4	11.8	1.00	-	-	-
mild	17	16	94.1	1	5.9	1	5.9	0.58	0.06	5.57	.64
moderate	104	87	83.7	17	16.3	19	18.3	1.96	0.58	6.63	.28
severe	40	25	62.5	15	37.5	16	40.0	4.46	1.29	15.43	**.02**

(Continues)

TABLE 3 (Continued)

	Discharged alive (ICU)			Death in ICU		Death at follow-up		Univariate analysis			
	N	n	%	n	%	n	%	HR	95% CI		*P*
Kidney injury (S-UREA)											
S-UREA < 10 mmol/L (ref)	173	147	85.0	26	15.0	26	15.0	1.0	-	-	-
S-UREA 10-29.9 mmol/L	39	28	71.8	11	28.2	16	41.00	3.48	1.82	6.63	**<.01**
S-UREA ≥ 30 mmol/L	4	1	25.0	3	75.0	3	75.00	7.23	2.17	24.07	**<.01**
Systolic BP											
< 70 mm Hg	13	9	69.2	4	30.8	7	53.9	3.80	1.50	9.60	**<.01**
70-99 mm Hg	99	82	82.8	17	17.2	19	19.2	1.10	0.60	2.20	.70
100-199 mm Hg (ref)	97	80	82.5	17	17.5	17	17.5	1.0	-	-	-
≥ 200 mm Hg	8	6	75.0	2	25.0	2	25.0	1.50	0.40	6.70	.60
Therapy											
Mechanical ventilation											
Yes	187	149	79.7	38	20.3	41	21.9	1.57	0.56	4.39	.39
No (ref)	30	28	93.3	2	6.7	4	13.3	1.00	-	-	-
Renal replacement											
Yes	32	15	46.9	17	53.1	18	56.2	4.69	2.57	8.57	**<.01**
No (ref)	185	162	87.6	23	14.2	27	14.6	1.00	-	-	-
Vasoactive infusion											
Yes	171	136	79.5	35	20.5	39	22.8	1.66	0.70	3.94	.25
No (ref)	46	41	89.1	5	10.9	6	13.0	1.00	-	-	-

The bold values show significant value.

[a] "Any chronic lung disease" denotes any combination of "chronic lung disease" and "asthma".

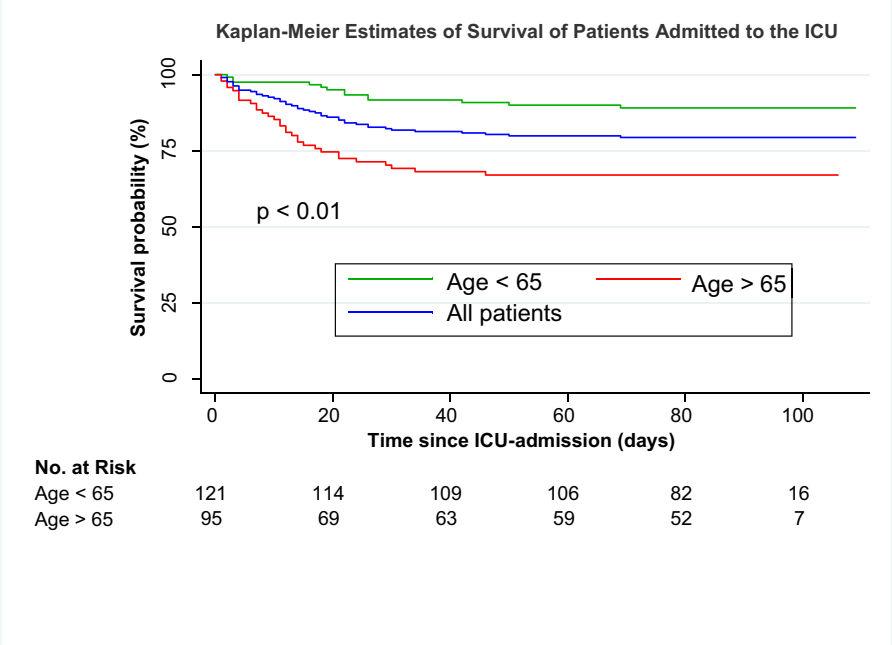

FIGURE 2 Survival estimates. Kaplan Meier estimates of survival of patients admitted to the ICU. Survival is reported for the overall group (blue) and by age (<65 years old [green] and ≥ 65 years old [red]). The analysis includes patients who survived the first day of intensive care (216 pts)

ill patients to proceed according to established routines and with experienced staff.

In this cohort of 217 SARS CoV2 positive patients admitted to Norwegian ICUs between March 10-June 19, ICU mortality was 18.4% (20.3% in MV patients). This compares favourably with early reports of very high mortality rates in critically ill COVID-19 patients,[10,12,15,16] and aligns with reports from other countries and regions with early and effective lockdown-policies or a low disease burden.[17-20,31] ICU LOS was prolonged, and associated with male gender, severity of respiratory failure at admission and being classified as ARDS.

Case-mix is a strong determinant of mortality in critically ill populations. Age and sex, co-morbidities and frailty are non-modifiable risk factors in patients with ARDS.[7] In this Norwegian cohort, such risk factors were roughly similar to those observed in other populations,[13,32] with a high prevalence of cardiovascular disease, diabetes and obesity, but our data suffer from an absence of data on the severity of co-morbid conditions. The small number of patients in our cohort precludes detailed analysis of the impact of all relevant risk factors. Age, diabetes and chronic kidney disease were all independently associated with mortality. Notably, however, the median age of our population was 63 years, similar to that observed in Italy[13] and intermediate of that observed in Denmark (68 years)[33] and Iceland (64 years),[34] and that found in Sweden (61 years),[35] and the UK (60 years).[32] It should be noted that admission to intensive care of nursing home residents is rarely deemed appropriate in Norway. In our cohort, the median clinical frailty scale[36] was 2 ("well") but was too infrequently reported to be included in analysis.

Severity of acute respiratory failure and other organ manifestations at admission was associated with mortality and LOS in the ICU. The median SAPS II-score recorded was 33, ie, lower than we anticipated and indicating that in Norway, the individual disease burden (or severity of illness) of critically ill covid-19 patients was relatively low. A median NEMS-score at 34.6 per day in the ICU also reflects a moderate number of interventions in our cohort but does not accurately reflect the nurse:patient ratio, which is never less than 1 in a Norwegian ICU. Whereas the median LOS in Norwegian ICUs is 2.0 days,[24] median ICU LOS for the COVID-19 cohort was 14.0 days. Taking into consideration these patients were managed under strict isolation, that a median of 12.0 days were spent on MV and that 38.2% of patients required MV in the prone position for a median of 5 days, resource utilization was considerable.

Potentially preventable or modifiable risk factors in severe respiratory failure are ventilator management (causing secondary lung injury) and extrapulmonary organ failures that may be influenced by patient management.[7] The Scandinavian Society of Anaesthesiology and Intensive Care Medicine (SSAI) has issued evidence-based guidelines for the management of patients with ARDS,[3,4] as well as fluid- and vasoactive drug management in the critically ill.[37-39] In webinars organised by Norwegian health authorities early March, the importance of adherence to these and/or similar guidelines[5] was highlighted, with a strong emphasis on the principles of pressure- and volume limitation, fluid management and avoidance of nephrotoxins.

A majority of Norwegian COVID-19 patients were managed with mechanical ventilation and vasoactive support, and only

TABLE 4 Outcomes (A) Mortality by premorbid patient characteristics–multivariable analysis. (B) Mortality by illness severity at admission–multivariable analysis

Risk factor	HR	95% CI		*P*
A				
Age ≥ 65 years	3.01	1.52	5.95	**<.01**
Cardiovascular disease	1.07	0.56	2.07	.83
Diabetes	2.41	1.29	4.52	**.01**
Chronic lung disease	1.28	0.63	2.58	.49
Chronic kidney disease	2.89	1.31	6.35	**.01**
B				
AHRF				
Not mechanically ventilated	1.00	-	-	-
Mild	0.35	0.04	3.21	.35
Moderate	1.22	0.41	3.65	.72
Severe	2.47	0.79	7.77	.12
Kidney injury (s-urea)				
S-UREA < 10 mmol/L (ref)	1.00	-	-	-
S-UREA 10-29.9 mmol/L	3.89	2.02	7.50	**<.01**
S-UREA ≥ 30 mmol/L	5.60	1.20	26.23	**.03**
Systolic blood pressure				
<70 mm Hg	2.42	0.87	6.73	.09
70-99 mm Hg	1.00	0.49	2.06	.99
100-199 mm Hg	1.00	-	-	-
≥200 mm Hg	1.55	0.20	12.17	.68

The bold values show significant value.

Abbreviations: AHRF, acute hypoxaemic respiratory failure

TABLE 5 Resource utilisation

	N	Mean (SD)	Sum	% of LOS
ICU LOS (days)	217	17.4 (14.6)	3771.8	100.0
MV (days)	187	15.2 (12.8)	2840.9	75.3
NIV (days)	84	1.2 (1.4)	103.6	2.7
RRT (days)	32	10.5 (7.8)	335	8.9
ECMO (days)	2	17.5 (12.5)	35.0	0.9
NEMS	213	602.2 (517.5)	128 261	-

Abbreviations: ICU LOS, intensive care length-of stay; MV, mechanical ventilation; NIV, non-invasive ventilation; RRT, renal replacement therapy; ECMO, extracorporeal ventilation; NEMS, Nine equivalents of nursing manpower score.

14.7% needed RRT (Table 5). Need for vasoactive drugs in a majority of patients may presumably be explained by use of sedative drugs (and a consequential drop in blood pressure) in most mechanically ventilated patients, rather than manifest circulatory failure. Renal replacement therapy was used in a minority of patients and in only 8.9% of total bed days. This contrasts with reports from other regions (UK: 26%,[15] New York: 34%.)[40] but resonates with data reviewed by Gabarre and co-workers.[41] In patients with ARDS, the development of acute kidney injury (AKI) portends a severe prognosis.[42] In New York, Chan and co-workers found AKI to be prevalent in ICU-patients with COVID-19 and associated with a high risk of death (in-hospital mortality 52%).[40] In a single-centre study in Modena, Italy, Alfano et al found AKI to be significant predictor of all-cause mortality.[43] This is in agreement with an observed ICU-mortality rate of 53.1% in patients requiring RRT in our cohort.

4.1 | Strengths and limitations

This study is limited by the amount of data available for analysis. Firstly, a comparatively low mortality rate and small number of patients with COVID-19 admitted to Norwegian ICUs preclude any detailed statistical analysis of risk-factors. Secondly, the NIPaR registry does not record details on patient management or monitoring data and it only collects a small set of laboratory values. Specifically, very little data on ventilator settings are available for analyses. Moreover, because the timing of interventions is generally not available, modelling of the effects of interventions on mortality becomes difficult due to the risk of immortal time bias. Finally, some data were provided at the discretion of clinicians involved: The cause(s) for admission to the ICU and classification of ARDS were provided without any qualifying criteria. As in other observational studies, we believe ARDS may have been under-recognised in patients with moderate severity of disease and short LOS.[8]

The strength of this report is that it is an analysis of a comprehensive and complete national dataset that includes all COVID-19 patients admitted to Norwegian ICUs and therefore describes a cross-section of both patients and their management in Norwegian ICUs during the first phase of the pandemic.

5 | CONCLUSIONS

In this national cohort of COVID-19 patients admitted to Norwegian ICUs, acute hypoxaemic respiratory failure was the most common cause of admission to the ICU and severity of respiratory failure at admission was predictive of length of stay. Mortality was comparatively low and associated with age and chronic co-morbidities as well as severity of illness at admission.

CONFLICT OF INTEREST

All authors declared no conflict of interest.

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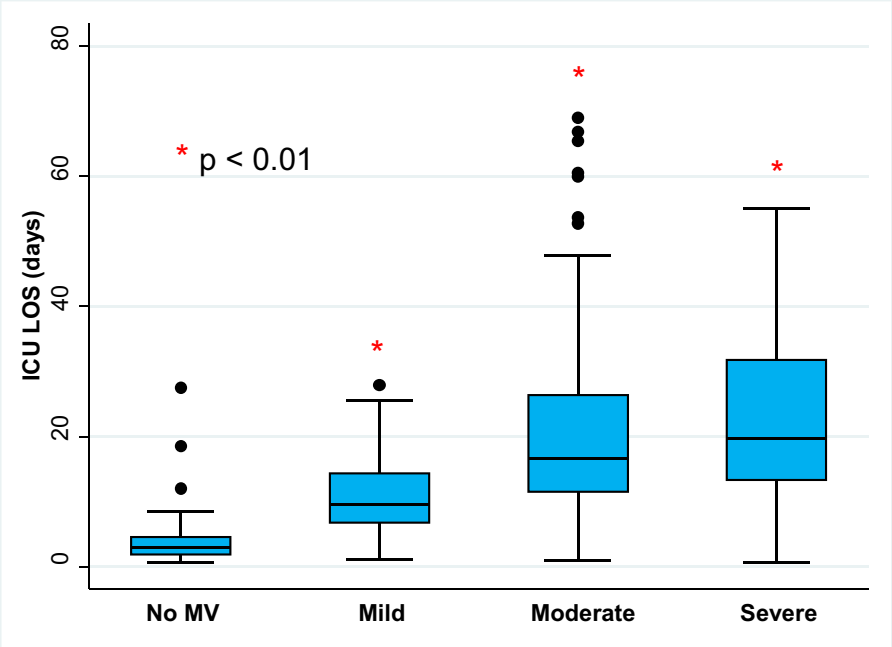

FIGURE 3 Length of stay. Length of stay (LOS) in the ICU by severity of respiratory failure at ICU admission. The boxplots illustrate LOS (days) for patients not requiring MV on the first day of admission, and MV patients with mild (pf-ratio > 26.6 kPa), moderate (pf-ratio > 13.3 and ≤ 26.6 kPa) or severe (pf-ratio ≤ 13.3 kPa) AHRF. LOS was significantly longer in patients requiring MV compared to patients who did not require MV and in patients with moderate or severe AHRF compared to those with mild AHRF. LOS was analysed with multiple linear regression (Appendix Table A5)

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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