

## Original Article

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# Characteristics and early outcomes of patients hospitalised for COVID-19 in North Zealand, Denmark

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## ABSTRACT

**INTRODUCTION:** Coronavirus disease 2019 (COVID-19) is an ongoing pandemic associated with significant morbidity and mortality worldwide. Limited data are available describing the clinical presentation and outcomes of hospitalised COVID-19 patients in Europe.

**METHODS:** This was a single-centre retrospective chart review of all patients with COVID-19 admitted to the North Zealand Hospital in Denmark between 1 March and 4 May 2020. Main outcomes include major therapeutic interventions during hospitalisation, such as invasive mechanical ventilation, as well as death.

**RESULTS:** A total of 115 patients were included, including four infants. The median age of adults was 68 years and 40% were female. At admission, 55 (50%) patients had a fever, 29 (26%) had a respiratory rate exceeding 24 breaths/minute, and 78 (70%) received supplemental oxygen. The prevalence of co-infection was 13%. Twenty patients (18%) (median age: 64 years; 15% female) were treated in the intensive care unit. Twelve (10.4%) received invasive mechanical ventilation and three (2.6%) renal replacement therapy. Nine patients (8%) developed pulmonary embolism. Sixteen patients (14%) died. Among patients requiring mechanical ventilation ( $n = 12$ ), seven (6.1%) were discharged alive, four (3.4%) died and one (0.9%) was still hospitalised.

**CONCLUSION:** In this cohort of hospitalised COVID-19 patients, mortality was lower than in other Danish and European case series.

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it causes, coronavirus disease 2019 (COVID-19), poses a serious threat to citizens, healthcare systems and societies worldwide.

One aspect that remains unclear is the difference in mortality rates between countries [1]. Factors reported to strongly impact the risk of dying from COVID-19 include male sex, advanced age and the presence of comorbidities, e.g., diabetes, hypertension and obesity [2-4]. The impact of these factors may vary between populations of different ethnic origins who are living in different settings and treated in different healthcare systems.

The first SARS-CoV-2 infection in Denmark was confirmed on 27 February 2020. Limited information is available describing the characteristics and outcomes of Danish patients requiring hospitalisation for COVID-19.

This study describes the clinical characteristics and outcomes of 115 sequentially hospitalised patients with COVID-19 in North Zealand Hospital, the Northern part of the Capital Region of Denmark.

## METHODS

We conducted a retrospective chart review of demographic and clinical data on patients with COVID-19 admitted to the North Zealand Hospital in Denmark between 1 March and 4 May

2020, with follow-up through 18 May 2020. Follow-up for survival was repeated in order to ensure a minimum of 30 days of survival follow-up. North Zealand Hospital is a 570-bed university-affiliated acute care hospital, delivering medical services to approximately 378,000 citizens in the Greater Copenhagen area. This study was approved by the institutional review board, by the Danish Data Protection Agency (approval number P-2020-472) and by the Danish Patient Safety Authority (project ID 31-1521-266). Due to the retrospective nature of the study, the requirement for informed consent was waived.

We included all consecutive patients hospitalised with confirmed SARS-CoV-2 infection by a positive result for real-time polymerase chain reaction (RT-PCR) testing [5] of an oropharyngeal swab or a lower respiratory tract specimen. Patients were considered to have confirmed infection if the initial test result was positive or if repeated testing was positive during the study period. Patients seen only in the emergency department and discharged in < 24 hours were excluded. Transfers from one regional hospital to another were merged and considered a single hospitalisation. For patients with readmission during the study period, data from the first admission were included.

Data were collected from the electronic medical record system and registered and managed using electronic data capture tools hosted by the Capital Region of Denmark [6, 7]. Two senior clinical doctors independently reviewed the data collection forms for accuracy.

The term admission tests refers to laboratory tests and imaging performed within the first 24 hours of admission.

Data analysis was mainly descriptive. Continuous variables were expressed as medians with interquartile range (IQR), and statistical comparisons were done with the Mann-Whitney U test. Categorical variables were expressed as number (%) and compared by Chi-squared test or Fisher's exact test between intensive care unit (ICU) care and non-ICU care groups. A two-tailed p value of < 0.05 was considered significant. All statistical analyses were performed using SPSS 24.0 and GraphPad Prism 8.0.0.

*Trial registration:* not relevant.

## RESULTS

### *Demographics and clinical presentation at admission*

A total of 115 SARS-CoV-2-positive patients were admitted from 1 March to 4 May 2020. Our cohort included four infants less than 12 months old, one 17-year-old child and 110 adults. Clinical characteristics and outcomes for the four infants are presented separately at the end of the Results section. The median age was 68.7 years (IQR: 56-78; range: 17-97) and 40% were female. The baseline characteristics for adult patients (17+ years) are summarised in **Table 1** including a comparison between patients with or without an ICU stay. The most

common comorbidities were hypertension (38; 34%), coronary artery disease (19; 17%) and diabetes (16; 14%). Eighty-one (73%) had at least one comorbidity. Ten (8.7%) patients had an immunocompromising condition. These conditions included nine with active malignancies and one solid organ transplant recipient. All patients treated in the ICU (n = 20) had at least one comorbidity. Patients treated in the ICU were more likely to be male, overweight or obese, have type 2 diabetes, have comorbidities and be treated with an angiotensin-converting enzyme inhibitor (ACEi) (Table 1).

**TABLE 1 /** Baseline characteristics of patients hospitalised with coronavirus disease 2019.

|   | All<br>(N = 111) | Non-ICU<br>(n = 91) | ICU<br>(n = 20) | p-value <sup>a</sup> |
|---|------------------|---------------------|-----------------|----------------------|
| <i>Demographic information</i>                                |                  |                     |                 |                      |
| Age, yrs:   |                  |                     |                 | 0.07                 |
| Median  | 68               | 69                  | 64              |                      |
| IQR   | 56-78            | 57-79               | 53-72           |                      |
| Range   | 17-97            | 17-97               | 33-85           |                      |
| Sex, female, n (%)  | 44 (40)          | 41 (45)             | 3 (15)          | 0.01                 |
| <i>Co-morbidities<sup>b</sup></i>                             |                  |                     |                 |                      |
| BMI, median, kg/m <sup>2</sup>                                | 26 (N = 100)     | 25 (n = 81)         | 29 (n = 19)     | 0.036                |
| Body weight, n (%):   |                  |                     |                 | 0.048                |
| Normal: BMI ≤ 25 kg/m <sup>2</sup>                            | 42               | 38 (47)             | 4 (21)          |                      |
| Overweight: 25 kg/m <sup>2</sup> < BMI ≤ 30 kg/m <sup>2</sup> | 31               | 25 (31)             | 6 (32)          |                      |
| Obese: BMI > 30 kg/m <sup>2</sup>                             | 27               | 18 (22)             | 9 (47)          |                      |
| Number of co-morbidities, n (%): <sup>c</sup>                 |                  |                     |                 | 0.002                |
| 0   | 30 (27)          | 30 (33)             | 0               |                      |
| ≥ 1   | 81 (73)          | 61 (67)             | 20 (100)        |                      |
| Cancer, n (%)   | 9 (8)            | 7 (8)               | 2 (10)          | 0.67                 |
| Hypertension, n (%)   | 38 (34)          | 29 (32)             | 9 (45)          | 0.30                 |
| Coronary artery disease, n (%)                                | 19 (17)          | 16 (18)             | 3 (15)          | 1.00                 |
| Congestive heart failure, n (%)                               | 8 (7)            | 7 (8)               | 1 (5)           | 1.00                 |
| Cerebrovascular disease, n (%)                                | 13 (12)          | 11 (12)             | 2 (10)          | 1.00                 |
| Asthma, n (%)   | 12 (11)          | 10 (11)             | 2 (10)          | 1.00                 |
| COPD, n (%)   | 8 (7)            | 8 (9)               | 0               | 0.35                 |
| Immunosuppression <sup>d</sup> , n (%)                        | 10 (9)           | 10 (11)             | 0               | 0.20                 |
| Chronic kidney disease, n (%)                                 | 8 (7)            | 5 (6)               | 3 (15)          | 0.15                 |
| Diabetes, n (%):  |                  |                     |                 |                      |
| T1D   | 2 (2)            | 1 (1)               | 1 (5)           | 0.33                 |
| T2D   | 14 (13)          | 8 (9)               | 6 (30)          | 0.02                 |

|                           |         |         |        |       |
|---------------------------|---------|---------|--------|-------|
| Subtotal                  | 16 (14) | 9 (10)  | 7 (35) | 0.009 |
| Ever smoked, n (%)        | 43 (39) | 36 (40) | 7 (35) | 0.80  |
| <i>Medications, n (%)</i> |         |         |        |       |
| ARBs                      | 16 (14) | 12 (13) | 4 (20) | 0.48  |
| ACEi                      | 8 (7)   | 4 (4)   | 4 (20) | 0.034 |

ACEi, = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II receptor blockers; COPD = chronic obstructive pulmonary disease; ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th rev.; ICU = intensive care unit; IQR = interquartile range, T1D = Type 1 diabetes; T2D = Type 2 diabetes.

a) Test for difference between non-ICU and ICU cohorts.

b) Defined as medical diagnoses included in medical history by ICD-10 coding.

c) Overweight/obesity not included as a co-morbidity in this number.

d) Defined as outpatient prescription of > 10 mg/day prednisolone or an equivalent steroid, use of chemotherapy, active malignancy or use of nonsteroidal immunosuppressive agents for solid organ transplant recipient or for an autoimmune disease.

At admission, half or more of patients presented with symptoms typical of respiratory tract infections (Table 2). The median time from onset of symptoms to hospital admission was eight days (IQR 4-13) (Figure 1). ICU patients were more likely to present with shortness of breath, had a lower oxygen saturation and more often received supplementary oxygen in triage. C-reactive protein (CRP) and creatinine were higher in ICU patients than in non-ICU patients: median CRP 109 versus 54 mg/L, median creatinine 89 versus 73 micromol/L. Abnormal chest imaging results were more common in patients requiring ICU admission: 95% versus 70%.

**TABLE 2 /** Admission findings, interventions and outcomes for patients hospitalised for coronavirus disease 2019.

|   | All<br>(N = 111) | Non-ICU<br>(n = 91) | ICU<br>(n = 20)  | p-value <sup>a</sup> |
|---|------------------|---------------------|------------------|----------------------|
| <i>Admission symptoms, n (%)</i>  |                  |                     |                  |                      |
| Cough, dry  | 82 (74)          | 65 (71)             | 17 (85)          | 0.27                 |
| Shortness of breath   | 86 (77)          | 67 (74)             | 19 (95)          | 0.04                 |
| Fever: $\geq 38^{\circ}\text{C}$  | 55 (50)          | 46 (51)             | 9 (45)           | 0.81                 |
| <i>Vital signs at admission</i>   |                  |                     |                  |                      |
| Body temperature, median (IQR), $^{\circ}\text{C}$                                | 37.8 (37.1-38.6) | 37.9 (37.2-38.6)    | 37.8 (36.9-38.7) | 0.74                 |
| SaO <sub>2</sub> , %, median (IQR)  | 96 (93-98)       | 96 (94-98)          | 93 (80-96)       | 0.003                |
| SaO <sub>2</sub> < 94%, n (%)   | 33 (30)          | 22 (24)             | 11 (55)          | 0.006                |
| Received supplementary O <sub>2</sub> at triage, n (%)                            | 78 (70)          | 59 (65)             | 19 (95)          | 0.001                |
| Respiratory rate, median (IQR), breaths/min.                                      | 20 (18-24)       | 20 (18-24)          | 20 (18-32)       | 0.31                 |
| Respiratory rate > 24/min., n (%)   | 29 (26)          | 21 (23)             | 8 (40)           | 0.16                 |
| <i>Laboratory results at admission</i>  |                  |                     |                  |                      |
| Leukocytes, concentration, median (IQR), $\times 10^9/\text{l}$ (N = 110)         | 6.0 (4.7-7.8)    | 5.9 (4.8-7.7)       | 6.5 (4.8-10.5)   | 0.48                 |
| Fibrin D-dimer concentration, median (IQR), $\mu\text{g}/\text{ml}$ (N = 77)      | 1.2 (0.7-2.4)    | 1.2 (0.6-2.4)       | 1.2 (1.0-1.8)    | 0.53                 |
| CRP concentration, median (IQR), mg/l (N = 110)                                   | 58 (25-108)      | 54 (21-92)          | 109 (55-148)     | 0.004                |
| HbA <sub>1c</sub> concentration, median (IQR), mmol/mol (N = 75)                  | 39 (37-46)       | 39 (36-45)          | 43 (38-51)       | 0.28                 |
| Glucose concentration, median (IQR), mmol/l (N = 107)                             | 6.9 (6.1-8.0)    | 6.9 (6.0-8.0)       | 7.1 (6.7-8.7)    | 0.09                 |
| Plasma creatinine concentration, median (IQR), $\mu\text{mol}/\text{l}$ (N = 110) | 77 (64-98)       | 73 (61-96)          | 89 (79-102)      | 0.009                |

|  |                 |                 |                      |       |
|--|-----------------|-----------------|----------------------|-------|
| PaO <sub>2</sub> , median (IQR), kPa (N = 74)                          | 9.2 (8.2-10.6)  | 9.6 (8.5-10.8)  | 8.2 (7.6-9.4)        | 0.009 |
| Ferritin concentration, median (IQR), ng/ml (N = 97)                   | 619 (316-1,420) | 607 (239-1,270) | 975 (460-1,638)      | 0.12  |
| <i>Chest radiograph findings<sup>a</sup></i>                           |                 |                 |                      |       |
| Diffuse/patchy bilateral infiltrates, n (%) (N = 107)                  | 83 (75)         | 64 (70)         | 19 (95)              | 0.04  |
| <i>Outcomes and interventions</i>                                      |                 |                 |                      |       |
| ARDS <sup>b</sup> , none/mild/moderate/severe, n (%)                   | -               | -               | 1/0/8/11 (5/0/40/55) | -     |
| Low-dose corticosteroid for COVID-19-induced ARDS <sup>c</sup> , n (%) | -               | -               | 5 (25)               | -     |
| Use of prone positioning for ARDS, n (%)                               | -               | -               | 5 (25)               | -     |
| Acute kidney injury <sup>d</sup> , n (%)                               | 13 (12)         | 7 (8)           | 6 (30)               | 0.01  |
| Cardiomyopathy, n (%)  | 0               | -               | -                    | -     |
| Acute hepatic injury <sup>e</sup> , n (%)                              | 0               | -               | -                    | -     |
| Non-invasive ventilation, n (%)  | 5 (5)           | 1 (1)           | 4 (20)               | 0.004 |
| Invasive mechanical ventilation, n (%)                                 | 12 (11)         | -               | 12 (60)              | -     |
| Evidence of co-infection <sup>f</sup> , n (%)                          | 14 (13)         | 12 (13)         | 2 (10)               | 1.00  |
| CT-angiography performed on suspicion of PE, n (%)                     | 16 (14)         | 9 (10)          | 7 (35)               | 0.009 |
| PE, n (%) <sup>g</sup>   | 9 (8)           | 4 (4)           | 5 (25)               | 0.009 |
| Fibrin D-dimer level at time of PE, median (IQR), FEU mg/l             | 10 (5.6-18.6)   | 10 (4.7-19)     | 12.4 (5.65-30.9)     | 1.00  |
| ECMO, n (%)  | 2 (2)           | -               | 2 (10)               | -     |
| RRT, n (%)   | 3 (3)           | 0               | 3 (15)               | 0.005 |
| Survived to transfer out of ICU, n (%)                                 | -               | -               | 13 (65)              | -     |
| Died hospitalised, n (%)   | 16 (14)         | 11 (12)         | 5 (25)               | 0.16  |
| Death directly related to COVID-19, n (%)                              | 14 (13)         | 9 (10)          | 5 (25)               | 0.13  |
| Discharged from hospital alive, n (%)                                  | 90 (81)         | -               | -                    | -     |
| Remains hospitalised at end of follow-up, n (%)                        | 5 (5)           | -               | -                    | -     |
| Re-admitted during study period, n (%)                                 | 10 (9)          | -               | -                    | -     |

ARDS = acute respiratory distress syndrome; COVID-19 = coronavirus disease 2019; CRP = C-reactive protein; ECMO = extracorporeal membrane oxygenation; ESICM = *European Society of Intensive Care Medicine*; FEU = fibrinogen equivalent units; HbA1c = glycated haemoglobin; ICU = intensive care unit; IQR = interquartile range; KDIGO = Kidney Disease: Improving Global Outcomes; PCR = polymerase chain reaction; PE = pulmonary embolism; RRT = renal replacement therapy; PaO<sub>2</sub> = O<sub>2</sub> arterial pressure; SaO<sub>2</sub> = O<sub>2</sub> arterial saturation.

a) Radiographic findings were based on the radiology report in the electronic medical record.

b) ARDS was defined according to the Berlin Criteria [8].

c) Low-dose corticosteroid for COVID-19-induced ARDS were administered according to ESICM's guidelines [9].

d) Acute kidney injury was based on the KDIGO definition [10].

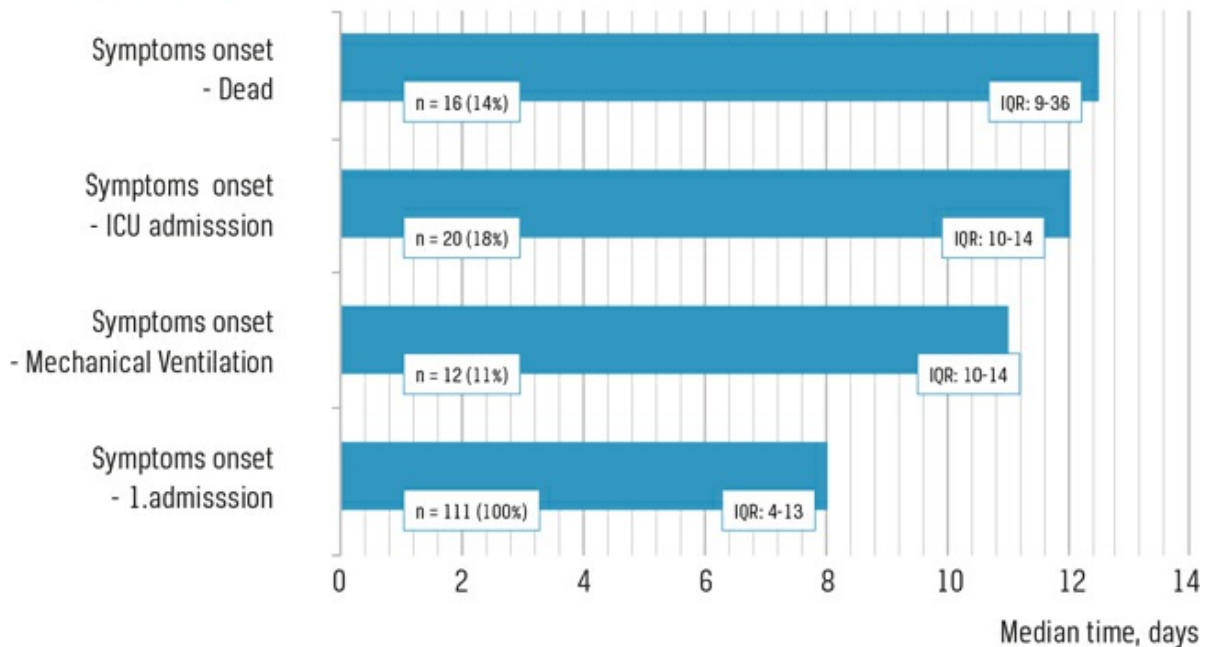
e) Acute hepatic injury was defined as an elevation in aspartate aminotransferase or alanine aminotransferase of > 15 times the upper limit of normal.

f) Criteria used for identifying co-infections were: 1) positive culture or PCR, 2) sample acquired within 3 days of hospitalisation, 3) clinically relevant, i.e. likely to contribute to symptomatology and guided treatment. See Supplementary Table 1 for details.

g) See Supplementary Table 2 for details.



**FIGURE 1 /** Timeline of coronavirus disease 2019 cases after onset of illness.



n = number of patients; ICU = intensive care unit; IQR = interquartile range.

### *Disease course and outcome*

During hospitalisation, 20 patients (18%) (median age 64 years, IQR 53-71; 15% female) were treated in the ICU, 12 (11%) received invasive mechanical ventilation, three (3%) were treated with renal replacement therapy and two (2%) were treated with extracorporeal membrane oxygenation (Table 2). Sixteen patients (14%) died (median age 83 years, range 53-97; 31% female). The rate of co-infection was 13% and did not differ significantly between groups (Table 2 and [Supplementary Table 1](#)). Patients treated in the ICU experienced more COVID-19 complications, including acute kidney injury (30% versus 7%) and pulmonary embolism (PE) (25% versus 4%). All observed PEs involved peripheral arteries. Eight out of nine patients experiencing a PE were male ([Supplementary Table 2](#)).

Seven patients (6%) participated in a randomised blinded trial of remdesivir. Eighty-four (76%) patients were discharged to their own home and six (5%) were discharged to a nursing facility. As of 18 May 2020, for patients requiring mechanical ventilation (n = 12), seven were discharged alive, four died and one remained admitted to hospital. A total of ten patients (9%) were readmitted during the study period. The median length of hospitalisation for all patients was six days (IQR 3-14).

### *Infants: presentation, clinical characteristics and outcome*

A total of four SARS-CoV-2-positive infants were admitted in the study period. Their age was between three weeks and ten months, 50% were female. None suffered from underlying

comorbidities. All were born at term. On admission, three infants (three months of age and below) had a temperature over 38.5 °C and were admitted due to fever of unknown cause. All three presented with diarrhoea and two of them were neutropenic, both heavily exposed to SARS-CoV-2 in the family. Only one had minor respiratory symptoms: cough for five days. All were discharged to their home and the three youngest recovered fully after initial hospitalisation. One infant (ten months of age) who was hospitalised due to seizures was not febrile at any time during the hospitalisation and was readmitted after two weeks due to renewed seizures.

## DISCUSSION

In our cohort of sequentially hospitalised patients with confirmed COVID-19, we found a high proportion of males, 65+ years of age, and patients with one or more comorbidities. This matches data from the United States, Italy and China [2-4, 8]. Comorbidity has been associated with a more severe disease course and with death in COVID-19 patients [9]. In line with this, the patients requiring ICU treatment in our study were more likely to suffer from comorbidities, e.g. diabetes, and were more often overweight and obese. Yet, none of the comorbidities were independently associated with a poorer outcome in our study.

We found that fever and respiratory tract symptoms were common in patients admitted with COVID-19, as also previously reported [8, 10]. Many patients had symptoms for 1-2 weeks before admission to hospital. Some patients appeared to experience a severe exacerbation of the disease late in the disease course, which distinguishes COVID-19 from other common infectious diseases.

The clinical manifestations observed in children in our study ranging from mild respiratory symptoms to mainly gastrointestinal symptoms and fever and a high recovery rate are in accordance with previously published reports [11].

Approximately one in six patients were transferred to the ICU for more intensive treatment and monitoring. If equated to the fraction of patients with a critical illness, this proportion is smaller than what has been reported in other case series of similar size from Europe and the United States [12-14]. Our data are comparable to those of reports from the European Centre for Disease Prevention and Control (ECDC), suggesting 15% of patients hospitalised for COVID-19 are transferred to the ICU (ECDC accessed 27-5-2020). The reported variations may be due to different admission practices between countries. Furthermore, some frail older patients are not transferred to the ICU because this is considered futile.

In our case series, the rate of co-infection was 13% (Table 2 and Supplementary Table 1). This is similar to previously reported rates in the 14-24% range [10, 12]. The incidence of co-infection has not been reported in previous Danish case series [13, 15].

Respiratory tract infection is a known risk factor in the development of PE in hospitalised



patients. Thrombotic complications in patients with COVID-19 are emerging as important sequelae that contribute to significant morbidity and mortality [16]. We report an overall PE incidence of 8% and 25% in ICU patients. The rate of PE in our cohort is lower than in a recent French study (n = 137) where the overall incidence of PE was 24% in all COVID-19 patients and 50% in COVID-19 patients treated in the ICU [16].

Among patients requiring intubation for mechanical ventilation, prone positioning for ARDS was only used in 25% of ICU patients. In a previous report from New York, prone positioning for ARDS was used in 50% of ICU patients with COVID-19 [10]. Our results are not unlike those found in a recent case series from Northern California [12]. Our results might indicate less severe ARDS in our ICU patients.

Our overall mortality rate of 14.4% was markedly lower than in two other Danish COVID-19 case series: Israelsen et al. reported an overall mortality rate of 24.6% and Pedersen et al. reported a mortality rate among ICU patients of 43% [13, 15]. Our mortality rate is also noticeably lower than those reported by several large case series from other countries [3, 4]. However, our results are comparable to recent case series from Northern California [8, 12] and New York City [17]. In part, this difference in death rates might be attributed to non-surge conditions. Patient volumes did not exceed normal operating capacity in our hospital during the study period. This could lead to patients being admitted who might not merit hospitalisation in conditions where hospital beds are limited. The lower mortality rates reported in our study compared to other Danish cohorts might also be a result of a different case mix. When comparing baseline characteristics to previous Danish case series [13, 15], we found that our population was younger, had a lower Body Mass Index (BMI) and a lower admission creatinine level. Furthermore, co-morbidities such as hypertension, diabetes and cardiovascular disease were less frequent. Advanced age and the presence of comorbidities such as diabetes, hypertension and obesity have previously been reported to strongly influence the risk of dying from COVID-19 [2-4].

The 25% death rate for ICU patients was also lower than previously reported rates from the United States where large studies from New York City reported mortality rates of 45–88% [4, 18]. Recent Danish reports described mortality rates of 43-59% [13, 15] for ICU patients with COVID-19. Comparisons between series must be made with caution due to variable populations and small sample sizes.

In our population, only 20 patients were 80 years or older. This may be attributable to limited spread of infection in this age group during the first part of the outbreak. The spread of infection among the oldest patients may be lower or delayed in Denmark compared with, e.g., Italy. Fewer elderly people live in institutions there, and more live in multi-generational homes or are cared for by younger family members.

The major limitations of our study include its retrospective nature and restriction to a single large hospital. Overall case numbers were low, probably because of early and decisive

public health interventions in our country. Because of the low number, the results must be interpreted with caution. The study was conducted during the early phase of the COVID-19 outbreak in Denmark. Key factors were changing over this period, including implementation of physical distancing measures and testing criteria, which could affect future results. Several of the patients were young and fit without comorbidity, which we believe is because the first phase of the COVID-19 outbreak in Denmark featured many cases imported from popular vacation destinations.

In conclusion, this case series provides characteristics and early outcomes of 115 sequentially hospitalised patients with confirmed COVID-19 in the North Zealand Region of Denmark. The manifestations of COVID-19 were comparable to those seen in other reports. However, we found the overall death rate and the death rate for ICU patients to be lower than those reported in two previous Danish case series.

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**CONFLICT OF INTEREST:** Disclosure forms provided by the authors are available with the full text of this article at [Ugeskriftet.dk/dmj](http://Ugeskriftet.dk/dmj)

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