Low mortality of hospitalised patients with COVID-19 in a tertiary Danish hospital setting

Lone Wulff Madsen[a,b,c,*], Susan Olaf Lindvig[a], Line Dahlerup Rasmussen[a],
Fredrikke Christie Knudtzen[a,c,d], Christian B. Laursen[c,e], Anne Øvrehus[a,c],
Stig Lønberg Nielsen[a], Isik Somuncu Johansen[a,c]

[a] Department of Infectious Diseases, Odense University Hospital, Odense, Denmark
[b] Open Patient data Explorative Network, Odense University Hospital, University of Southern Denmark, Odense, Denmark
[c] Department of Clinical Research, University of Southern Denmark, Odense, Denmark
[d] Clinical Center of Emerging and Vector-borne Infections, Odense University Hospital, Denmark
[e] Department of Respiratory Medicine, Odense University Hospital, Denmark

A B S T R A C T

Objectives: We aimed to describe clinical characteristics and outcomes of admitted COVID-19 patients in a Danish hospital setting where an early active government intervention was taken.
Methods: This prospective cohort study included all patients admitted to the COVID-19 unit at Odense University Hospital from March 10 to April 21, 2020. Patients were assessed by a multidisciplinary team at admission. Outcome parameters were development of acute respiratory distress syndrome (ARDS), intensive care unit (ICU) admission, death and admission time.
Results: We included 83 patients (median age 62 years, 62.7% male). At hospitalization, 31.3% needed oxygen supplementation and the median National Early Warning Score was four. Median admission time was 7 days (Interquartile ranges (IQR) 3−12). In total, ARDS was diagnosed in 33.7% (28/83) of the patients, corresponding to an incidence rate of 7.1 per 100 person days (95% CI: 4.1−10.2). Overall 13 patients (15.7%) were transferred to the ICU, of whom 11 (84.6%) received corticosteroids. No patients died while admitted to the ICU. Four patients (4.8%) died during admission.
Conclusion: Despite similar patient characteristics compared to those reported by others, we found a low overall mortality of < 5%.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has caused a major worldwide health crisis and it is essential to learn more about the disease and its management. Publications from the most severely affected regions have demonstrated substantial variation in patient characteristics, disease course, and treatment outcome (Colaneri et al., 2020; Guan et al., 2020; Lechien et al., 2020; Richardson et al., 2020). The political engagement, the socio-demography of affected population and the preparedness of health care facilities of the individual countries appear to affect the course of the pandemic (Docherty et al., 2020; Grasselli et al., 2020; Habib, 2020; Ihle-Hansen et al., 2020; Israelsen et al., 2020; Stafford, 2020; Steffens, 2020). Organization of the health care system and its capacity seems to play a key role in the management of the patients and treatment outcomes (ECDC, 2020). The Danish social and health care system is tax funded and provides equal access to free universal healthcare and government sponsored compensation in the event of unemployment or illness.

The first Danish case of COVID-19 was reported on February 26, 2020 (SSI, 2020c). The initial spread of the infection was believed to be from returning Danish ski tourists from epicenters in Northern Italy and Austria, but within a few weeks local transmission was evident. On March 11 the Danish government locked down large sections of the Danish society to reduce further spread of the infection. At that time, Denmark had 514 confirmed COVID-19 cases in a country with 5.8 million inhabitants, which corresponded to 8.9 cases per 100,000 population (Danmarks

Statistik. Population statistics 2020 Population statistics, Office, 2020). The epidemic in Denmark peaked at the end of March - early April, with the highest number of admitted COVID-19 patients registered on April 1 2020 (9.2 patients per 100,000 population including 2.5 patients per 100,000 population in the intensive care units (ICU)) (SSI, 2020a). After the lockdown, the number of new COVID-19 cases requiring admission has steadily declined leading to the first phase of the re-opening of the society, which was launched on April 15. On May 7, the number of total admitted patients to Danish hospitals was as low as 145 and the second phase of the re-opening of the society was announced (Police, 2020; SSI, 2020b). So far, there is little information about COVID-19 from countries with a social and health structure comparable to Denmark.

The overall aim of this prospective observational cohort study was to report the clinical characteristics and outcome of hospitalized patients with COVID-19 in a tertiary Danish hospital setting, with special focus on patients admitted to the ICU and patients with and without ARDS. In addition, we will report on the model of care for COVID-19 and the capacity within our health system.

Methods

Setting

The study was performed at Odense University Hospital (OUH), which serves both as a community hospital for approximately 500,000 persons and as a tertiary hospital for the Region of Southern Denmark (approximately 1.2 million inhabitants)(Danmarks Statistik. Population statistics). In the beginning of the epidemic, all COVID-19 patients admitted in the Region of Southern Denmark, who were deemed clinically stable for transportation, were transferred to a dedicated corona unit at OUH for further therapy. A substantial number of healthcare personal was trained. The strategy was aimed to provide each COVID-19 unit all necessary basic skills in e.g. lung, heart or neurological disease. This ensured that the allocated staff cared for patients with COVID-19 with co-morbidities within their area of expertise, assisted by Infectious Disease (ID) specialists, thereby building on existing capacity and forming multidisciplinary teams (MDT). The core members of the team of responsible physicians for the COVID-19 patients comprised ID physicians, pulmonologists, intensive care specialists and nephrologists.

Study design

A hospital-based prospective cohort study.

COVID-19 management

COVID-19 management was based on local and national guidelines and consisted primarily of supportive therapy (OUH). The indication for steroid treatment was moderate to severe (ARDS) and use of steroids was based on an MDT consensus where standard treatment was dexamethasone 20 mg iv for 5 days followed by 10 mg for a further 5 days. No other therapy was given unless patients were included in randomized clinical trials (RCTs). Upon admission, each patient was evaluated by a senior consultant and an intensive care specialist to determine whether the patient was a candidate for ICU treatment and/or resuscitation based on the patient`s wishes along with a combination of age, comorbidities or conditions that may limit the potential for future rehabilitation. Based on this evaluation, patients who developed severe respiratory failure or multi-organ failure during admission were either transferred to the ICU or kept on the COVID-19 unit for further therapy.

Population

We included all patients who 1) were 18 years or older, 2) had a positive real time polymerase chain reaction (RT-PCR) analysis for SARS- CoV-2 performed on material from a pharyngeal swab or tracheal secretion indicating COVID-19 disease, and 3) were admitted or transferred to OUH between March 10 - April 21. At end of follow-up for this study (May 1), all patients except one were either dead or discharged.

The COVID-19 baseline date was defined as the day of admission for patients presenting with COVID-19 symptoms, or the first date of a positive RT- PCR analysis of SARS-CoV-2 for already hospitalised patients who developed symptoms of COVID-19 during admission.

Data collection

A review of the patients' electronic medical record (EMR) was performed in order to obtain demographic, clinical, laboratory, management and outcome data. Comorbidity was defined as both current and past diseases; for further details see supplemental 1. All triage values (temperature, oxygen saturation with and without supplemental oxygen, blood pressure and heart rate) were registered, and based on these values National Early Warning Scores version 2 (NEWS2) were calculated for each patient (Physicians, 2017). Based on the EMR, the Eastern Cooperative Oncology Group (ECOG) performance status was derived for each patient (Oken et al., 1982).

All relevant data were registered in a database by one investigator and subsequently checked by a second member of the study team. In case of discrepancy, a consensus was reached through discussion among team members. A complete codebook was predefined for all variables (supplemental 1). All blood samples were registered from the laboratory system to the database.

Outcome definitions

The following clinical defined outcomes were considered:

1) ARDS: The criteria for ARDS and grading of severity of ARDS was based on the fraction of the partial pressure of oxygen (PaO2) to the fraction of inspired oxygen (FiO2) (PaO2/FIO2-ratio) and results of chest imaging as described in current international recommendations (Ferguson et al., 2012; Griffiths et al., 2019).

2) ICU admission: Date of transfer to and discharge from the ICU as well as any supportive care given during ICU admission

3) Length of admission to ICU: Total time from transfer to discharge from ICU

4) Length of admission: Discharge from a COVID-19 unit ≤/> 7days

5) Death: Date and cause of death

Statistics

Descriptive statistics were reported as proportions for categorical variables and medians with interquartile ranges (IQR) for continuous variables depending on the data distribution.

Time was computed from COVID-19 baseline (as previously defined) until date of the outcome of interest or May 1, whichever came first. For all outcomes, the number, proportion and time to the outcome as well as median time was computed. We used Cox regression analyses to compute incidence rates (IR) and 95% confidence intervals (CI). We used cumulative incidence function

to illustrate time to first occurrence of ARDS stratified by gender, body mass index ((BMI) $</\geq$25) and age $</\geq$ 70, respectively. To identify predictors for ARDS we used Cox regression to compute incidence rate ratios (IRR) as a measure of the relative risk. In the univariate model we examined potential risk factors for ARDS (age $</\geq$70, sex, BMI $</\geq$25, comorbidity and ECOG performance score). In the multivariate model we restricted the analyses to age and gender, which remain the most important variables in risk analyses of morbidity and mortality, and further included variables with p-value <0.1. Finally, Pearson correlation was used to investigate whether there was a correlation between age and admission time.

Table 1

Demographic characteristics of patients admitted to Odense University Hospital with COVID-19.

Study population	No. (%)
No. of patients	83
Age (years), median (IQR)	62 (54–74)
18–49	14 (16.9)
50–64	32 (38.6)
65–79	22 (26.5)
≥80	15 (18.1)
Sex	
Male	52 (62.7)
Female	31 (37.3)
Ethnicity	
Caucasian	70 (84.3)
Non-Caucasian	13 (15.7)
BMI, median (IQR)	26.5 (23.7–30.1)
<25	28 (34.2)
≥25- <30	33 (40.2)
≥30	21 (25.6)
Smoking	
Current smoker	5 (6.1)
Former smoker	32 (39.0)
Never smoker	45 (54.9)
Units of alcohol per week	
>7 for women / >14 for men	5 (6.1)
≤7 for women / ≤14 for men	77 (93.9)
Comorbidity	
Any cardiovascular disease	46 (55.4)
Hypertension	35 (42.2)
Atrial fibrillation	13 (15.7)
Ischemic heart disease	7 (8.4)
Valvular heart disease	6 (7.2)
Congestive heart failure	5 (6.0)
Stroke	4 (4.8)
Peripheral vascular disease	3 (3.6)
Chronic pulmonary disease	14 (16.9)
Malignancy	14 (16.9)
Diabetes mellitus I+II	13 (15.7)
Inflammatory bowel disease	3 (3.6)
Rheumatoid arthritis	3 (3.6)
Chronic kidney disease	2 (2.4)
Medication prior to admission	
Antibiotic therapy	30 (36.1)
ACE inhibitor / ARBs	31 (37.4)
Immunosuppressive	7 (8.4)
ECOG Performance score	
0	55 (66.3)
1	16 (19.3)
2	5 (6.0)
3	6 (7.2)
4	1 (1.2)
Time from onset of symptoms to admission (days), median (IQR)	9 (5.5–11)
Initial hospital of admission	
OUH	41 (49.4)
Community-hospital	42 (50.6)

Abbreviations: Odense University Hospital (OUH), Angiotensin-converting enzyme (ACE), Angiotensin II receptor blockers (ARBs), Eastern Cooperative Oncology Group (ECOG), Body Mass Index (BMI).
Data on BMI, smoking and alcohol were available for 82/83 patients. Data on time from onset of symptoms to admission were available for 80/83 patients.

Data management

Prospective data from all COVID-19 patients were registered in a REDCap database hosted by Open Patient data Explorative Network (OPEN). STATA version 15 (Stata Corp LP, Texas) was used for data processing and analyses.

Approvals

This study is approved as a quality study and registered on the Region of Southern Denmark's record of data processing activities (j. nr. 20/16,169). All data are handled in accordance with applicable laws: The General Data Protection Regulation (GDPR), the Danish Act on Data Protection, the Danish Act on Research Ethics Review of Health Research Projects and the Danish Health Act.

Table 2

Clinical parameters at admission for patients admitted to Odense University Hospital with COVID-19.

Study population	No. (%)
No. of patients	83
Symptoms	
Fever	75 (90.4)
Cough	71 (85.5)
Dyspnea	58 (69.9)
Headache	44 (53.0)
Myalgia	44 (53.0)
Fatigue	38 (45.8)
Nausea/vomiting	32 (38.6)
Dizziness	24 (28.9)
Diarrhea	24 (28.9)
Chest pain	14 (16.9)
Abdominal pain	13 (15.7)
Throat pain	11 (13.3)
Rhinitis	9 (10.8)
Change of taste	9 (10.8)
Change of smell	5 (6.0)
Vital signs	
Temperature, median (IQR)	38.4 (37.7–39.0)
<37.5	16 (19.3)
37.5–38.0	18 (21.7)
38.1–39.0	29 (34.9)
>39.0	20 (24.1)
Respiratory rate (breaths per minute), median (IQR)	20 (18–24)
≤24	65 (78.3)
>24	18 (21.7)
Saturation(%) without supplemental oxygen, median (IQR)[a]	95 (92–97)
<92	17 (20.5)
≥92	66 (79.5)
Received supplemental oxygen	26 (31.3)
- Nasal cannulae	21 (80.8)
- Mask with or without bag	5 (19.2)
Supplemental oxygen with nasal cannulae (liters/minute), median (IQR)	2 (1.5–3.0)
Systolic blood pressure (mmHg), median (IQR)	134 (121–147)
≤ 90	2 (2.4)
Heart rate (beats per minute), median (IQR)	87 (77–99)
>130	4 (4.8)
Glasgow Coma Scale	
15	82 (98.8)
<15	1 (1.2)
National Early Warning Score 2, median (IQR)	4 (3–6)
0–4 (low)	42 (50.6)
5–6 (medium)	21 (25.3)
>6 (high)	20 (24.1)

Abbreviations: Interquartile range (IQR).
[a] Data on saturation without supplemental oxygen were available for 78 patients.

Results

Between March 10 and April 21, we included 83 patients in the study, of whom 50.6% were transferred from other hospitals. Three patients were diagnosed with COVID-19 during admission for non-COVID-19 related illnesses.

Patient characteristics

Baseline characteristics of the study population are shown in Table 1. The median age was 62 years (Interquartile range; IQR 54–74), 62.7% were men and 84.3% were Caucasian. The median Body Mass Index (BMI) was 26.5 (IQR 23.7–30.1) and 25.6% were obese (BMI ≥ 30). In total, 54.9% were never smokers and five (6.1%) had a high alcohol consumption. More than half of the admitted COVID-19 patients had prior cardiovascular diseases (CVD) (55.4%) of which hypertension was the most dominant (42.2%). Other common comorbidities included chronic pulmonary diseases (16.9%), malignancies (16.9%), and diabetes (15.7%). Although a total of 86.8% had at least one comorbidity, the majority of the patients (66.3%) had an ECOG performance score of 0 before onset of disease. The median duration of symptoms prior to hospitalization was 9 days (IQR: 5.5–11.0 days).

Clinical status at admission

The most frequent symptoms at admission were fever (90.4%), cough (85.5%) and dyspnea (69.9%) (Table 2). At the initial triage, 59.0% had a temperature ≥38.1 degrees Celsius and 21.7% had a

Table 3
Laboratory and radiological findings at admission for patients admitted to Odense University Hospital with COVID-19.

Tests in study population	Value, median (IQR)	Reference values	No. of patients tested (n=83)
Haemoglobin[a] (g/dl)	13 (12.6–14.8)	Female 11.8–15.3 Male 13.4–16.9	83
White-cell count (10^9/L)	6.8 (5.2–8.6)	3.50–8.80	83
Neutrophils (10^9/L)	4.4 (3.2–6.7)	1.50–7.50	83
Lymphocytes (10^9/L)	0.86 (0.63–1.31)	1.00–4.00	79
Monocytes (10^9/L)	0.47 (0.33–0.72)	0.20–0.80	79
Basophiles (U/L)	0.04 (0.04–0.04)	<0.20	79
Eosinophils (10^9/L)	0.04 (0.04–0.06)	<0.50	79
Platelets (10^9/L)	188 (163–254)	Female 165–400 Male 145–350	82
C-reactive protein (mg/L)	66 (29–112)	<6.0	83
Pro-calcitonin (μg/L)	0.15 (0.06–0.21)	<0.10	21
Ferritin (μg/L)	496 (201–1017)	Female≤ 15–180 Female > 50 years 15–450 Male 15–560	27
D-dimer (mg/L)	0.87 (0.39–1.87)	< 55 years <0.50 55–65 years <0.60 65-75 years <0.70 >75 years <0.80	64
Fibrinogen (μmol/L)	16.0 (13.2–18.5)	5.2–12.6	48
Lactate dehydrogenase (U/L)	294 (212–357)	<70 years 105–205 >70 years 115–255	66
Alanine aminotransferase (U/L)	33 (24–50)	Female 10–45 Male 10–70	79
Creatine kinase (U/L)	104 (55–197)	Females 35–210 Male 18–50 years 50–400 Male >50 years 40–280	57
Creatinine (μmol/L)	84 (68–99)	Female 45–90 Male 60–105	83
Urea (mmol/L)	5.6 (4.3–7.8)	Female 18–50 years 2.6–6.4 Female >50 years 3.1–7.9 Male 18–50 years 3.2–8.1 Male >50 years 3.5–8.1	62
Albumin (g/L)	38 (35–41)	< 40 years 36-50 40-70 years 36–48 >70 years 34–45	82
Activated partial thromboplastin time (APTT) (s)	26 (24–28)	22–28	57
International Normalized Ratio (INR)	1.06 (1.00–1.17)	<1.20	79
Pancreatic amylase (U/L)	34 (22–51)	10–65	55
Bilirubin (μmol/L)	8 (6–10)	5–25	81
Troponin T (ng/L)	8 (7–22)	<14	16
Potassium (mmol/L)	3.8 (3.6–4.1)	3.5–4.4	81
Sodium (mmol/L)	136 (134–139)	137–145	83
Lung opacities on chest x-ray	No. (%)		81
Unilateral	13 (16.1)		
Bilateral	41 (50.6)		
None	27 (33.3)		
Pleural Effusion	10 (12.4)		
Placement of opacity			
Right upper lobe	33 (40.7)		
Right middle lobe	32 (39.5)		
Right lower lobe	44 (54.3)		
Left upper lobe	29 (35.8)		
Left lower lobe	42 (51.9)		
Microbiology results during admission	No. positive / tested persons	No. positive/total tests	
Sputum culture[b]	27/60 (45.0)	54/123 (43.9)	
PCR for Legionella pneumophila, Mycoplasma Pneumoniae and Chlamydia pneumoniae	0/46 (0)	0/60 (0)	
PCR for influenza virus	0/65 (0)	0/71 (0)	
Blood culture	4/80 (5.0)	14/208 (6.7)	
Urine culture	3/66 (19.7)	22/143 (15.4)	
Faeces (PCR/culture)	2/19 (10.5)	2/26 (7.0)	
Cerebrospinal fluid (PCR/culture)	0/1 (0)	0/2 (0)	

Abbreviations: Interquartile range (IQR), Polymerase Chain Reaction (PCR).
[a] Hemoglobin; mmol of hemoglobin/L. Conversion factor from g/dL to mmol/L is 0.6202.
[b] In 70.4% (38/54) the positive sputum cultures included yeast.

respiratory rate greater than 24 breaths/min. At admission 31.3% needed oxygen therapy (80.8% via nasal cannula (median oxygen supplementation 2 L/min) and 19.2% on a mask with or without bag). Although 49.4% had a NEWS2 score of >4, less than 5% were hemodynamically unstable at presentation (systolic blood pressure ≤90 mmHg and/or heart rate >130 bpm).

Paraclinical status at admission

Laboratory and radiological findings at admission are summarized in Table 3. Notable values with medians outside of normal reference range included lymphocyte count (0.86×10^9/L), C-reactive protein (66 mg/L), ferritin (496 μg/L), d-dimer (0.87 mg/L), fibrinogen (16.0 μmol/L) and lactate dehydrogenase (294 U/L). Reference values are shown in Table 3. Almost all patients (97.5%) had a chest x-ray performed upon admission and of these, 66.7% had lung opacities. Pleural effusion was rare (12.4%). The pneumonic opacities were randomly distributed in all pulmonary lobes.

Most patients had blood cultures performed and four patients had clinically relevant bacteremia with *Klebsiella pneumoniae*, *Escherichia coli*, *Enterococcus faecalis* or *Staphylococcus lugdunensis*.

Sputum cultures were performed in 45% (27/60) of the patients, of which 16 patients (59.3%) only had yeast. Only 11 patients had culture-verified bacterial pneumonia with *Haemophilus influenza* (n = 2), *Streptococcus pneumoniae* (n = 2) and *Staphylococcus aureus* (n = 7).

Outcome

ARDS

ARDS criteria were met in 33.7% (28/83) of the patients, corresponding to an incidence rate of 7.1 per 100 person days. Of these, 25% (7/28) were characterized as severe ARDS. Of the patients transferred to the ICU, 92.3 (12/13) were diagnosed with ARDS, of which 41.7% (5/12) was characterized as severe. Overall, 75% (21/28) of the patients with ARDS were men. We found no difference in median age between patients with severe ARDS and patients without ARDS. Of patients with ARDS, 57.1% (4/7) received immunosuppressive treatment prior to the COVID-19 admission (supplemental 2a). As shown in Figure 1, we found a trend towards a higher cumulative incidence for ARDS for male gender, age ≤70 years and a BMI ≥ 25; however, this was not statistically significant (rank test >0.05). We found a moderately positive correlation between admission time and age (Pearson's correlation coefficient r = 0.32, p = 0.003). When investigating predictors for ARDS, male sex, BMI ≥ 25 and prior cardiovascular morbidity showed a trend towards an increased risk of ARDS in the univariate analyses, but none of the variables were deemed statistically significant (supplemental 3). In the multivariate analysis, cardiovascular comorbidity was associated with a statistically significant more than 2.6 times higher risk of ARDS (supplemental 3).

ICU admission

At admission, 81.9% (68/83) were evaluated to be candidates for treatment in the ICU and 13 patients (15.7%) were transferred to the ICU. Median time from hospitalization until ICU admission was 1 day (range 0–10 days) and from onset of symptoms until ICU admission was 10 days (range 4–24 days). Almost all patients (92.3%) received mechanical ventilation. Only one patient received noninvasive ventilation at the ICU. The median age was 63 years (IQR 60–69) and the majority was male (76.9%). The average number of comorbidities was 2.5 (range 1–4), the most frequent being hypertension (61.5%) (Supplemental Table 2b). None of the ICU patients died, and by the end of the study period, all but one patient was discharged from hospital.

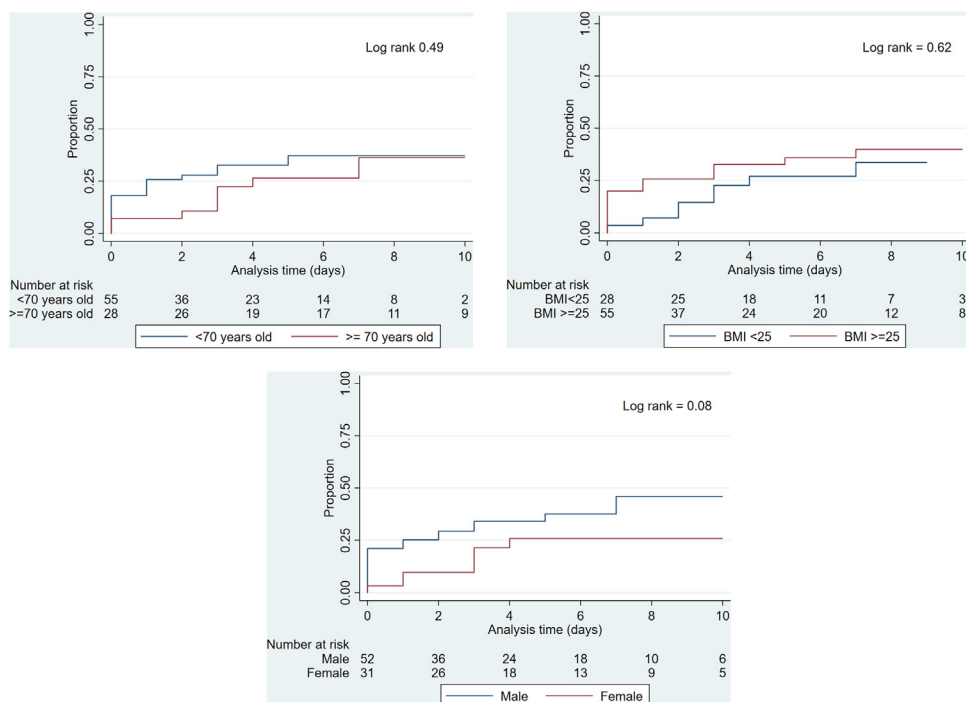**Figure 1.** Cululative incidence for ARDS stratified by (a) gender, (b) age < / ≥ 70 years old, and (c) BMI < / ≥ 25.
Abbreviations: ARDS; Adult respiratory distress syndrome, BMI; Body Mass Index. (Pearson's correlation coefficient r = 0.32, p = 0.003)

Table 4
Outcomes in patients admitted to Odense University Hospital with COVID-19.

Study population	No. (%) N=83	Person days at risk	Median person days at risk (IQR)	Incidence rate per 100 person days (95% CI)
No. of patients	83			
ARDS	28 (33.7)	395	4.0 (2−9)	7.1 (4.1−10.2)
ARDS				
Mild	14 (50)			
Moderate	7 (25)			
Severe	7 (25)			
In-hospital mortality of ARDS patients	2 (7.1)			
ICU candidate at admission				
Yes	68 (81.9)			
No	15 (18.1)			
ICU	13 (15.7)	354	4.0 (2−8)	3.7 (2.1−6.3)[a]
Invasive mechanical ventilation	12 (92.3)			
Vasopressors	12 (92.3)			
Renal replacement therapy	4 (30.8)			
ECMO	0 (0)			
In-hospital mortality of ICU patients.	0/13 (0)			
Time in ICU (days), median (IQR)	11 (IQR, 7−12)			
Status on May 1, 2020				
Died during admission	4 (4.8)	794	7.0 (4−12)	0.5 (0.2−1.3)
Discharged alive from hospital	78 (94)			
Still admitted in hospital	1 (1.2)			
Time from hospital admission to dead (days), median (IQR)	10 (6.5−13)			
Time from hospital admission to discharge (days), median (IQR)	7 (3−12)[b]			
Therapy during admission				
Steroids for ARDS	10 (36)			
Antibiotic therapy during admission	69 (83.1)			
Piperacillin-tazobactam	53 (63.9)			
Amoxicillin-clavulanate	37 (44.6)			
Meropenem	14 (16.7)			
Benzylpenicillin	12 (14.5)			
Macrolide	6 (7.2)			
Other[c]	20 (24.1)			

Abbreviations: Number of patients (No.), Interquartile range (IQR), adult respiratory distress syndrome (ARDS), intensive care unit (ICU), extracorporeal membrane oxygenation (ECMO).
[a] IR for ICU is only calculated for the 68 ICU candidates.
[b] Only calculated for the 82 patients whom were either dead or discharged at the end of follow-up.
[c] Other, name (No. of patients): Fluconazol (5), Cefuroxim (3), Amoxicillin (2), Dicloxcillin (2), Ciprofloxacin (2), Metronidazol (2), Mecillinam (1), Vancomycin (1), Nitrofurantoin (1), Aciclovir (1).

Treatment

Antibiotic therapy was prescribed empirically to 69 (83.1%) patients during hospitalization, of whom 74.7% of the patients received broad-spectrum antibiotics (piperacillin-tazobactam, meropenem, cephalosporines, Table 4). Steroids were prescribed to 35.7% (10/28) of the patients with ARDS. In total, 8 patients received dexamethasone, of which all were admitted to the ICU and diagnosed with either moderate or severe ARDS. In addition, 3 patients admitted to ICU received another high dose of corticosteroids.

Admission time and course of disease

Median time of hospital stay until discharge was 7 days (IQR 3−12 days). The patients hospitalized for more than seven days had a higher median age (67 versus 58 years) and had more cardiovascular comorbidities (70.8% versus 34.3%, supplemental table 2c).

We found an overall low mortality rate of 0.5 per 100 person days (95%CI: 0.2−1.3). The four patients who died (4.8%) during admission had a median age of 83, of whom 75% were men (Supplemental 2d). Cause of mortality was respiratory failure in all cases. The median time of hospital stay until death was 10 days (IQR 6.5−13 days) (Table 4).

Health system capacity

During the study period, neither the regular COVID-19 units nor the ICU were at maximum capacity at any time. In the ICU, patients were cared for by the regular ICU staff at all times.

Discussion

This Danish hospital-based prospective cohort study is among the first to report COVID-19 data from a Scandinavian country where all inhabitants have free and equal access to health care and social support. The general patient characteristics in our study are similar to those reported by others with 17% requiring admission to the ICU (Docherty et al., 2020) and the same proportion of ARDS (Zhou et al., 2020), however, we still found a low overall mortality of 4.8% and a mortality of 0% among patients treated in the ICU. This illustrates the excellent set-up with 1) high preparedness, 2) use of MDTs, and 3) the widespread use of dexamethasone for ARDS. These results are from a period in which the Danish government launched an aggressive lockdown of the society to reduce the spread of SARS-CoV-2. As it is apparent from the reduction of COVID-19 admissions during the study period, this lockdown was successful in reducing the number of COVID-19 admissions in Denmark. As a result, our tertiary center never got overwhelmed with severely ill COVID-19 patients.

As observed in studies from other countries, the COVID-19 patients in need of hospital admission in this study were predominately male, overweight, and middle-aged to elderly with frequent co-morbidities, in particular cardiovascular diseases (Goyal et al., 2020; Grasselli et al., 2020; Zhou et al., 2020). Regarding clinical symptoms, vital signs, and laboratory findings, we found no substantial difference between our results and findings in other studies (Pascarella et al., 2020; Wang et al., 2020). The patients' NEWS2 scores appeared to be higher in our cohort (Carr et al., 2020); however, the score is not frequently used in other studies.

ARDS has previously been reported as one of the most frequent causes of deterioration in COVID-19, with reported proportions between 15.6–30.0% (Li and Ma, 2020). Despite similar proportions of ARDS in our study, an overall low mortality was found among admitted patients when compared to other countries (Suleyman et al., 2020; Zhou et al., 2020). One of the reasons for this may be the use of corticosteroids to 84.6% of the ICU patients. A randomized clinical trial and meta-analysis that since have been published have shown that use of dexamethasone or systemic corticosteroids in general reduces mortality for critically ill patients (Horby et al., 2020; Sterne et al., 2020). Our population had a low ECOG performance score at admission. This might be a result of self-isolation of elderly persons and patients with many comorbidities, as advised by the government in early March. As such, one could speculate that this could also have contributed to the overall low mortality. Although no statistically significant association between the ECOG score and ARDS was found in the univariate and multivariate regression analyses, these analyses are affected by lack of power. In addition, we found a moderately positive correlation between admission time and age independently of ARDS risk. This could indicate that the inverse relation between age and risk of ARDS was due to an increased admission time among patients with a higher age.

The preparedness of each country and the characteristics of the population have shown to be predictors of the overall mortality (Chaudhry et al., 2020).

Results from the same period from another Danish hospital and a large German study illustrated a mortality of above 20%; however, the median ages in these cohorts were somewhat higher than ours (Israelsen et al., 2020; Karagiannidis et al., 2020). As our institution had composed an MDT of doctors, all COVID-19 patients were triaged by specialists in ID, respiratory medicine and anesthesiology to ensure that fragile patients were not admitted to the ICU. Furthermore, decision on initiation of steroid treatment for ARDS was based on MDT consultations. However, in this context, it is worthy of note that among those deemed too fragile for the ICU, only four patients died. We speculate that our MDT approach led to better evaluation and treatment of the patients.

Strengths and limitations

A major strength of this study is that it was performed in a country with free and equal access to health care. All patients experiencing symptoms and signs of COVID-19 infection could be seen quickly by a skilled physician and admitted to hospital if deemed necessary. Therefore, the patients in this study were probably in a better overall condition compared with patients from other settings. Another strength of this study is the MDT approach and the early recognition of the need for development of regional standardized guidelines for the management of COVID-19 patients, which secured best practice treatment. Finally, empirical therapy with antiviral or immunosuppressive drugs was not given outside RCTs. The exception was steroid therapy for ARDS, for which the decision to treat was based on MDT discussions.

The major limitation of this study is the small sample size and single center setting which to some degree may limit its generalizability. Moreover, the low sample size restricted the number of variables that could be included in the regression models in order to avoid an over-fitted model.

Furthermore, the low ECOG score and lower median age when compared to other cohorts from comparable studies complicates comparison.

Conclusion

This study provides characteristics of Danish hospitalized COVID-19 patients. Despite similar proportions of ARDS in our study, an overall low mortality was found among admitted patients when compared to other countries. This suggest that the preparedness of the society and a timely and well-prepared strategy with an MDT approach to COVID-19 patients along with the use of dexamethasone may improve patient management and short-term prognosis, including need of ICU treatment.

Statement of role

ISJ conceived the study with input from all co-authors. LWM, SOL, FCK, CBL, SLN collected the data. SLN did the data analyses and SLN, LWM and LDR performed the interpretation of the data. LWM and ISJ wrote the first draft of the manuscript and all authors contributed to the final version.

Declaration of interest

Lone Wulff Madsen, Susan Olaf Lindvig, Line Dahlerup Rasmussen, Fredrikke Christie Knudtzen, Anne Øvrehus, Christian B. Laursen, Stig Lønberg Nielsen, Isik Somuncu Johansen declares no conflict of interest.

Role of founding source

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2020.10.018.

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