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Clinical characteristics and prognostic factors in COVID-19 patients aged ≥80 years

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Aim: The aim of the present study was to describe the clinical presentation of patients aged ≥80 years with coronavirus disease 2019 (COVID-19), and provide insights regarding the prognostic factors and the risk stratification in this population.

Methods: This was a single-center, retrospective, observational study, carried out in a referral center for COVID-19 in central Italy. We reviewed the clinical records of patients consecutively admitted for confirmed COVID-19 over a 1-month period (1–31 March 2020). We excluded asymptomatic discharged patients. We identified risk factors for death, by a uni- and multivariate Cox regression analysis. To improve model fitting and hazard estimation, continuous parameters where dichotomized by using Youden's index.

Results: Overall, 69 patients, aged 80–98 years, met the inclusion criteria and were included in the study cohort. The median age was 84 years (82–89 years is interquartile range); 37 patients (53.6%) were men. Globally, 14 patients (20.3%) presented a mild, 30 (43.5%) a severe and 25 (36.2%) a critical COVID-19 disease. A total of 23 (33.3%) patients had died at 30 days' follow up. Multivariate Cox regression analysis showed that severe dementia, pO_2 ≤90 at admission and lactate dehydrogenase >464 U/L were independent risk factors for death.

Conclusions: The present data suggest that risk of death could be not age dependent in patients aged ≥80 years, whereas severe dementia emerged is a relevant risk factor in this population. Severe COVID-19, as expressed by elevated lactate dehydrogenase and low oxygen saturation at emergency department admission, is associated with a rapid progression to death in these patients. **Geriatr Gerontol Int 2020; 20: 704–708.**

Keywords: COVID-19, dementia, older adults, prognostic factors.

Introduction

Since the first case was identified in Wuhan city (China) in December 2019, the novel coronavirus designated SARS-CoV-2, has caused an international outbreak of respiratory illness named coronavirus disease 2019 (COVID-19). The spectrum of COVID-19 is various, ranging from possible asymptomatic patients to severe progressive pneumonia and acute respiratory distress syndrome leading to death.[1–5]

After the first case of COVID-19 was diagnosed in the Lombardy region of Italy, in February, one of the largest and most serious clusters of COVID-19 in the world struck the Italian nation. Despite an aggressive effort of containment put in place, the disease continues to spread and the number of affected patients is still rising; furthermore, the case fatality rate has been very high and dominated by older patients.[6]

Italy presents one of the highest life expectancies in the world, which is at birth 80.3 years for men and 84.9 years for women.[7] In Italy, people aged >65 years now represent approximately 22.6% of the population, and older adults aged ≥80 years represent 6.5% of the total population.[7]

The overall estimated case fatality rate of COVID-19 in Italy is 7.2%; however, the median age for all COVID-19 related death is 81 years (73–86 years), and the case fatality rate in patients aged ≥80 years is >20%.[8] Nevertheless, up to now, limited data are available for COVID-19 in older patients, and no reports have focused on patients aged ≥80 years.[9–11]

The aim of the present study was to describe the clinical presentation of patients aged ≥80 years with COVID-19, and provide insights regarding the prognostic factors and the risk stratification in this distinctive population.

Methods

Study design

This was a single-center, retrospective, observational study carried out in an urban teaching hospital, which is a referral center for COVID-19, in central Italy. We reviewed the clinical records of all the patients aged ≥80 years consecutively admitted to our emergency department (ED) for suspected COVID-19 over a 1-month period (1–31 March 2020). COVID-19 was diagnosed based on the World Health Organization interim guidance.[12] We included

Table 1 Clinical and demographic characteristics of patients aged ≥80 years included in the study cohort

Variable	All population (n = 69)	Survived (n = 46)	Died (n = 23)	P
Age (years)	84 (82–89)	84 (81–89)	85 (83–86)	0.858
Sex (male)	37 (53.6%)	25 (54.3%)	12 (52.2%)	0.864
Ed presentation				
• Heart rate (min⁻¹)	85 (75–95)	83 (75–92)	87 (73–107)	0.404
• Systolic BP (mmHg)	127 (111–140)	130 (112–140)	122 (100–137)	0.132
• Diastolic BP (mmHg)	75 (65–89)	78 (65–90)	68 (60–86)	0.183
• pO₂ (%)	94 (90–96)	95 (93–96)	89 (82–94)	0.001
• Temperature (°C)	36 (35.5–36.5)	36 (35.5–36.5)	36.2 (35.7–36.8)	0.596
• GCS	15 (15–15)	15 (15–15)	15 (15–15)	0.202
• NEWS ≥3	41 (59.4%)	24 (52.2%)	17 (73.9%)	0.083
Symptoms				
• Fever	56 (81.2%)	56 (81.2%)	56 (81.2%)	0.663
• Dyspnea	32 (46.4%)	13 (28.3%)	19 (82.6%)	<0.001
• Cough	29 (42.0%)	22 (47.8%)	7 (30.4%)	0.168
• Fatigue	8 (11.6%)	6 (13.0%)	2 (8.7)	0.595
• Other	11 (15.9%)	7 (15.2%)	5 (21.7%)	0.500
Clinical history				
• CHF/CAD	21 (30.4%)	14 (30.4%)	7 (30.4%)	1.000
• Hypertension	41 (59.4%)	31 (67.4%)	10 (43.5%)	0.057
• Cerebrovascular disease	20 (29.0%)	11 (23.9%)	9 (39.1%)	0.189
• Diabetes	9 (13.0%)	7 (15.2%)	2 (8.7%)	0.448
• COPD	7 (10.1%)	3 (6.5%)	4 (17.4%)	0.159
• Severe dementia	8 (11.6%)	2 (4.3%)	6 (26.1%)	0.014
• Malignancy	3 (4.3%)	2 (4.3%)	1 (4.3%)	1.000
• Living in institution	17 (24.6%)	11 (23.9%)	6 (26.1%)	0.843
Radiology				
• Negative	8 (11.6%)	7 (15.2%)	1 (4.3%)	
• Monolateral pneumonia	29 (42.0%)	20 (43.5%)	9 (39.1%)	0.302
• Bilateral pneumonia	32 (46.4%)	19 (41.3%)	13 (56.5%)	
Severity classification				
• Mild	14 (20.3%)	13 (28.3%)	1 (4.3%)	
• Severe	30 (43.5%)	22 (47.8%)	8 (34.8%)	0.005
• Critical	25 (36.2%)	11 (23.9%)	14 (60.9%)	
Outcome				
• ICU admission	11 (15.9%)	4 (8.7%)	7 (30.4%)	0.034
• Survival time (days)	26 (11–35)	35 (32–39)	5 (2–13)	–
• Deaths	23 (33.3%)			–

P-values are shown with regard to comparison between patients who survived and died. Survival follow up was assessed at 30 days from emergency department admission. BP, blood pressure; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; GCS, Glasgow Coma Scale; ICU, intensive care unit; NEWS, National Early Warning Score; pO₂, peripheral oxygen saturation.

in the analysis only patients with a positive result on real-time reverse transcription polymerase chain reaction assay of nasal and pharyngeal swab specimens.

We excluded from the study cohort patients discharged from ED, and patients already on orotracheal intubation at ED arrival. For patients with more than one admission, only the latest access was included in the analysis.

Study variables

We extracted from computerized clinical records clinical, laboratory and radiological findings at admission. We included in the analysis the following:

• Physiological parameters: age, sex, temperature, heart rate, respiratory rate, blood pressure, Glasgow Coma Scale score, oxygen supplementation and peripheral oxygen saturation (pO₂). Based on physiological parameters, we calculated the National Early Warning Score for all patients.

• Symptoms at admission: fever (core temperature >37.5°C), dyspnea, cough, fatigue or other (including sore throat, headache, diarrhea, abdominal pain, dysgeusia).

• Radiographic findings: based on chest X-ray or CT scan obtained in ED, patients were categorized as normal, monolateral ground-glass opacity or interstitial involvement and bilateral pneumonia.

• Laboratory findings: hemoglobin, total white cell blood count, serum creatinine, blood urea nitrogen, alanine aminotransferase, lactate dehydrogenase, fibrinogen, prothrombin time, D-dimer, ferritin, C-reactive protein (CRP) and procalcitonin.

• Patient disease presentation in ED: categorized as mild for normal X-ray findings, severe for positive S-ray and pO₂ ≥92%, and critical for positive X-ray and pO₂ <92%.

• Clinical history: coronary artery disease or congestive heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, severe dementia, malignancy and institution residency.

Table 2 Laboratory values of patients aged ≥80 years in the study cohort

Laboratory	Reference value	Entire population (*n* = 69)	Survived (*n* = 46)	Died (*n* = 23)	*P*
Haematology					
Hemoglobin (g/dL)	13.0–16.0	13.2 (11.9–14.5)	13.2 (11.9–14.3)	13.2 (11.7–14.7)	0.784
White cell blood count (x10⁹/L)	3.5–9.5	5.78 (4.55–7.67)	5.78 (4.83–7.50)	5.93 (3.94–8.27)	0.636
Biochemistry					
Creatinine (mg/dL)	0.67–1.17	1.05 (0.88–1.52)	1.03 (0.88–1.32)	1.45 (0.88–2.05)	0.068
Blood urea nitrogen (mg/dL)	10–23	22 (17–38)	20 (16–31)	39 (20–58)	0.006
Alanine aminotransferase (U/L)	7–45	19 (14–32)	18 (13–27)	21 (15–53)	0.175
Lactate dehydrogenase (U/L)	<250	322 (269–480)	305 (239–409)	511 (297–724)	0.005
Blood coagulation					
Prothrombin time (s)	11–13	11.3 (18.8–11.9)	11.2 (10.9–11.9)	11.4 (10.8–12.6)	0.678
Fibrinogen (mg/dL)	200–400	478 (375–551)	475 (372–530)	497 (394–649)	0.225
D-dimer (ng/mL)	<500	1446 (916–4729)	1374 (946–4824)	1875 (834–5090)	0.962
Inflammatory markers					
C-reactive protein (mg/dL)	<5	88.1 (33.2–156.7)	62.4 (28.1–102.6)	145.7 (77.9–210.5)	0.002
Procalcitonin (ng/mL)	<0.5	0.11 (0.00–0.35)[†]	0.06 (0.00–0.18)[†]	0.29 (0.11–0.55)[†]	0.001
Ferritin (ng/mL)	12–240	732 (493–1267)	721 (413–1302)	806 (566–1381)	0.888

The *P*-value comparison is shown for differences between patients who survived and patients who died.

[†]A total of 14 procalcitonin values are missing: nine among patients who survived and five among patients who died.
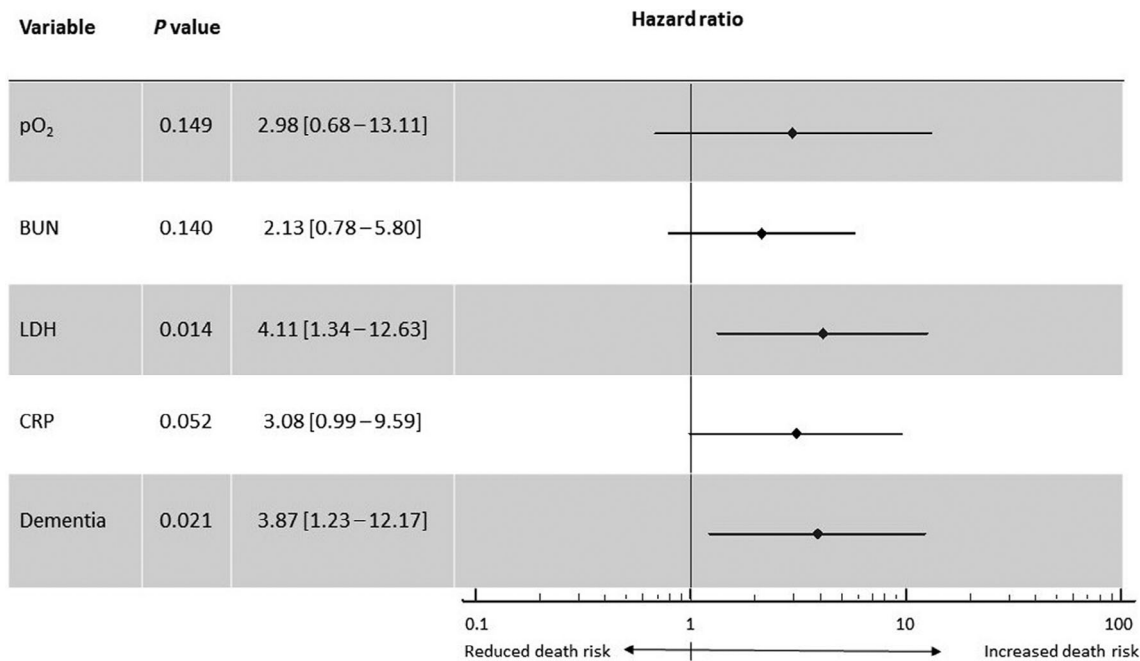
Figure 1 Multivariate Cox regression for prognostic factors. The forest plot graphically represents hazard ratios (95% confidence interval) for peripheral oxygen saturation (pO₂), blood urea nitrogen (BUN), lactate dehydrogenase (LDH), C-reactive protein (CRP) and dementia. All parameters were assessed at emergency department admission.

Study end-points

The primary study end-point was the patient's death. Survival follow up was assessed at 30 days from admission.

Statistical analysis

Continuous variables are reported as the median (interquartile range), and are compared at univariate analysis by Mann–Whitney *U*-test. Categorical variables are reported as the absolute number (percentage), and are compared by the χ^2-test (with Fisher's test if appropriate).

We compared the clinical and laboratory variables by a univariate Cox analysis (proportional hazards regression) for their association with survival. The post-hoc analysis was made by log–rank test. We entered significant parameters at univariate analysis into a multivariate Cox regression model to identify independent predictors of death. For a better model fitting and hazard estimation, we categorized the continuous variables into dichotomous parameters (i.e. low/high). For each variable, we obtained the optimal dividing cut-off by Youden's index, carrying out a receiver operating

characteristic (ROC) curve analysis with respect to association with death. Survival curves were estimated by the Kaplan–Meier method. We regarded a two-sided P-value ≤0.05 as significant. Data were analyzed by SPSS v25 (IBM, Chicago, IL, USA) and Medcalc 18.2 (MedCalc Software, Ostend, Belgium).

Statement of ethics

The study was carried out in accordance with the Declaration of Helsinki, and was approved by the local ethics committee.

Results

A total of 69 patients, aged 80–98 years, met the inclusion criteria and were included in the study cohort. The median age was 84 years (82–89 years is interquartile range); 37 patients (53.6%) were men. Globally, 14 patients (20.3%) presented a mild, 30 (43.5%) a severe and 25 (36.2%) a critical COVID-19 disease (Table 1). Overall, 23 patients died. Interestingly, the age and sex distribution were similar between the patients who survived and died (Table 1).

Clinical history was quite homogeneous among the patients, and the patients who survived did not present relevant differences compared with those who died. However, the patients who died presented more frequently a history of severe dementia (Table 1). As expected, the disease severity classification in ED was associated with outcome: among the patients who died, 14 (60.9%) had a critical, eight (34.8%) a severe and just one patient had a mild presentation. Disease progression was quite fast in the patients who died. The median survival time for non-survivors was 5 days (2–13 days is interquartile range).

Among physiological parameters at admission, pO_2 was the only parameter significantly associated with death in the present cohort. For as laboratory values, patients who died had higher blood urea nitrogen, lactate dehydrogenase, CRP and procalcitonin levels (Table 2). By using the ROC analysis with regard to these continuous variables, we found the best cut-off values discriminating death occurrence. Values were pO_2 ≤90% (AUC 0.748 [0.608–0.889], $P = 0.001$), blood urea nitrogen >37 mg/dL (AUC 0.680 [0.526–0.835], $P = 0.023$), CRP >112 mg/dL (AUC 0.717 [0.577–0.857], $P = 0.006$) and lactate dehydrogenase >464 U/L (AUC 0.708 [0.561–0.855]). The best discriminating value for procalcitonin was >0.19 ng/mL; however, we did not include it in the multivariate model, as we had 14 missing values.

Multivariate Cox regression analysis showed that severe dementia, pO_2 ≤90 at admission and lactate dehydrogenase >464 U/L were independent risk factors for survival in these patients (Fig. 1).

Discussion

The present study evaluated the clinical course and risk factors for patients aged >80 years affected by COVID-19. Our data suggest that for patients aged ≥80 years, further increasing age is not a risk factor for survival, whereas a history of severe dementia, low pO_2 at admission, high CRP and lactate dehydrogenase >464 U/L are risk factors for death.

Until 2002, four coronavirus were known to infect humans, and they globally accounted for 10–30% of upper respiratory tract infections in adults, with mild clinical consequences.[5,13] The outbreak of SARS-CoV and MERS-CoV caused international alarm, whereas the factors associated with transmission of these human coronaviruses remain poorly understood.[14,15] Similar to SARS-

CoV, the SARS-CoV-2 binds to human angiotensin-converting enzyme 2 (ACE2) for cell entry.[15,16] Angiotensin-converting enzyme 2 is a membrane protein expressed in the lung, heart, kidney and intestine. Angiotensin-converting enzyme 2 is largely expressed in the upper and lower respiratory tract, and this could explain both the infectivity and lethality of Sars-Cov2.[15]

There is clear evidence that older patients are at higher risk of death from COVID-19.[1–5,17–20] Italian national data show an overall mortality rate of 12.6%.[21] However, mortality steeply increases with age; for patients aged <50 years it is <1%, in the fifth decade it is 2.6%, in the sixth decade it is 9.8%, in the seventh decade it rises to 24.2% and in the eighth decade it rises to 29.0%. Interestingly, the mortality rate decreases to 24.7% in people aged ≥90 years.[20] The present data, although in a limited sample, appear to confirm this tendency. We found, in the present cohort of people aged ≥80 years, that increasing age does not represent a risk factor for death. Whether this is due to a minor susceptibility of patients aged >90 years to Sars-CoV-2 infection damage, or possibly to a reduced secondary lung inflammation, should be further investigated.

As the Sars-Cov2 cell entry receptor is located mainly in the lungs, more than half of patients might develop dyspnea, and >10% might require ventilatory support.[1–5,17–20] With acute hypoxia being the main determinant of disease progression and severity, the pO_2 at admission is crucial for death risk stratification. The present data confirm that patients aged ≥80 years who are severely hypoxic at ED admission (pO_2 <90%) have an increased risk of death. However, a pO_2 ≤90% was not associated with death in the present cohort at multivariate analysis. Certainly, the reduced sample and the subsequent wide confidence interval of our hazard estimation could not provide final clues on this point. Indeed, the present patients were mainly severe and critical at admission, thus reducing the relative influence of hypoxia on our final hazard estimation.

An elevation of lactate dehydrogenase in COVID-19 patients who died was found in most of the studies currently available.[22] These observations appear to be consistent with SARS, where multivariate analysis identified elevated lactate dehydrogenase as a marker associated with worse outcomes.[23] However, lactate dehydrogenase is a non-specific marker, which is commonly found in critically ill patients. Nevertheless, the present data confirm that >464 U/L could be a relevant prognostic factor in patients aged ≥80 years affected by COVID-19.

The CRP level correlates to inflammation, and its concentration is not affected by age, sex and physical condition.[24] CRP is a well-known index of severe pulmonary infections, and CRP levels were shown to positively correlate with lung lesions and disease severity in COVID-19.[1–5,25] The present data suggest that elevated CRP could have a predictive role in oldest-old patients with COVID-19; however, because of the small sample size in the present study, an association between elevated CRP and an increased risk of death cannot be established with certainty.

A distinct aspect of the present study is the association between dementia and poor outcome. Indeed, medical assistance to COVID-19 patients could be extremely difficult for patients with dementia.[26] First, the new hospital environment can lead to increased stress and behavioral problems in these patients.[27] Second, hypoxia, which is a prominent clinical feature of COVID-19, could complicate the presentation of dementia and induce delirium, increasing the need for medical care, and the need for dementia support.[28]

The outbreak of the COVID-19 pandemic has raised great concerns for the >50 million people living with dementia worldwide.[26] These people might have difficulties in remembering

safeguard procedures, such as wearing masks, and self-quarantine measures could not apply to patients who are not self-sufficient. Finally, long-term care facilities for dementia patients are at extreme risk for COVID-19 infection.[29] The present data suggest that severe dementia itself is an independent risk factor for survival in COVID-19 patients aged ≥80 years. Thus, as recommended by Alzheimer's Disease International, specific support for people living with dementia and their caregivers is urgently required, worldwide.[30]

As for any retrospective study, several limitations of the present study are worth considering. First, our sample size was small, thus limiting the power of our analysis. Furthermore, we carried out the study at a single institution, and as such, the findings might be not representative of the general population of COVID-19 patients aged ≥80 years . Finally, the study focused on patient deaths. For this reason, we cannot extrapolate relevant outcomes for this population, such as permanent need for oxygen support, loss of autonomy or the need to transfer to a residential nursing facility.

Patients aged ≥80 years are the most at risk of a poor outcome for COVID-19. Nevertheless, to date, scarce data are available about the distinctive expression of disease in this frailer part of the population. Although carried out in a small sample, the present study could give relevant clues on clinical risk factors for COVID-19 in patients aged ≥80 years. The present data suggest that the might could be not age dependent in this population. Furthermore, dementia appears to be one of the most relevant risk factors for death. Severe COVID-19, as expressed by elevated lactate dehydrogenase, elevated CRP and low oxygen saturation at admission, is associated with a rapid progression to death in these patients.

Disclosure statement

The authors declare no conflict of interest.

References

1 Guan WJ, Ni ZY, Hu Y *et al.* China medical treatment expert group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–1720. https://doi.org/10.1056/NEJMoa2002032 [Epub ahead of print].

2 Huang C, Wang Y, Li X *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, Chnia. *Lancet* 2020 (Feb 15); **395** (10223): 497–506.

3 Chen N, Zhou M, Dong X *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020 Feb 15; **395** (10223): 507–513.

4 Wang D, Hu B, Hu C *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 (Feb 7); **323**: 1061. https://doi.org/10.1001/jama.2020.1585. [Epub ahead of print].

5 Jin Y, Yang H, Ji W *et al.* Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses* 2020; **124**: 372.

6 Edward Livingston MD, Karen Bucher MA. CMI Coronavirus disease 2019 (COVID-19) in Italy. *JAMA* 2020; **323** (14):1335. https://doi.org/10.1001/jama.2020.4344.

7 ISTAT. Istituto Nazionale di Statistica. https://www.istat.it/it/archivio/94531 Accessed on April 30, 2020.

8 Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* (Mar 23) 2020; **323** (18): 1775–1776.

9 Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: a comparison with young and middle-aged patients. *J Infect* 2020 (Mar 27); **80** (6): e14–e18.

10 Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: a review of clinical data in China. *Mech Ageing Dev* 2020 (Apr 27); **118**: 111255.

11 Wang L, He W, Yu X *et al.* Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect* 2020 (Mar 30); **80** 6: 639–645.

12 World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. January 28, 2020 https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf Accessed on April 1 2020.

13 Paules CI, Marston HD, Fauci AS. Coronavirus infections-more than just the common cold. *JAMA* 2020 (Jan 23); https://doi.org/10.1001/jama.2020.0757.

14 Yu IT, Li Y, Wong TW *et al.* Evidence of airborne transmission of the severe acute respiratory syndrome virus. *N Engl J Med* 2004; **350** (17): 1731–1739.

15 Cao Y, Liu X, Xiong L, Cai K. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis. *J Med Virol* 2020 (Apr 3). https://doi.org/10.1002/jmv.25822.

16 Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020 Mar; **579** (7798): 270–273 Epub 2020 Feb 3.

17 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020 (Feb 24). [Epub ahead of print]. https://doi.org/10.1001/jama.2020.2648.

18 Grasselli G, Zangrillo A, Zanella A *et al.* Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* 2020; **323** (16): 1574–1581. https://doi.org/10.1001/jama.2020.5394.

19 Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of hospitalized adults with COVID-19 in an integrated health care system in California. *JAMA* (Apr 24) 2020;e207202. https://doi.org/10.1001/jama.2020.7202.

20 Richardson S, Hirsch JS, Narasimhan M *et al.* Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* (Apr 22) 2020; **323** 20: 2052–2059. https://doi.org/10.1001/jama.2020.6775.

21 ISS (Istituto Superiore di Sanità) https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_28-aprile-2020.pdf Accessed on May 1 2020.

22 Zhou F, Yu T, Du R *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020 (Mar 28); **395** (10229): 1054–1062 Epub 2020 Mar 11. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. Lancet. 2020 Mar 28;395(10229):1038. PubMed PMID: 32171076).

23 Leong HN, Earnest A, Lim HH *et al.* SARS in Singapore – predictors of disease severity. *Ann Acad Med Singapore* 2006; **35**: 326–331.

24 Chalmers S, Khawaja A, Wieruszewski PM, Gajic O, Odeyemi Y. Diagnosis and treatment of acute pulmonary inflammation in critically ill patients: the role of inflammatory biomarkers. *World J Crit Care Medl* 2019; **8** (5): 59–71.

25 Wang L. C-reactive protein levels in the early stage of COVID-19. *Med Mal Infect* 2020 (Mar 31); **50** 4: 332–334.

26 Wang H, Li T, Barbarino P *et al.* Dementia care during COVID-19. *Lancet* 2020 (Apr 11); **395** (10231): 1190–1191.

27 Kales HC, Lyketsos CG, Miller EM, Ballard C. Management of behavioral and psychological symptoms in people with Alzheimer's disease: an international Delphi consensus. *Int Psychogeriatr* 2019 Jan; **31** (1): 83–90.

28 Marcantonio ER. Delirium in hospitalized older adults. *N Engl J Med* 2017 (Oct 12); **377** (15): 1456–1466.

29 McMichael TM, Currie DW, Clark S *et al.* Epidemiology of COVID-19 in a long-term care facility in King County, Washington. *N Engl J Med* 2020 (Mar 27); **382** (21): 2005–2011.

30 Alzheimer's Disease International. ADI offers advice and support during COVID-19. 2020 (Mar 17). https://www.alz.co.uk/news/adi-offers-advice-and-support-during-COVID-19.