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**RESEARCH PAPER**

# Clinical profile and predictors of in-hospital mortality among older patients hospitalised for COVID-19

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## Abstract

**Background:** the coronavirus disease 2019 (COVID-19) is characterized by poor outcomes and mortality, particularly in older patients.

**Methods:** post hoc analysis of the international, multicentre, 'real-world' HOPE COVID-19 registry. All patients aged ≥65 years hospitalised for COVID-19 were selected. Epidemiological, clinical, analytical and outcome data were obtained. A comparative study between two age subgroups, 65–74 and ≥75 years, was performed. The primary endpoint was all cause in-hospital mortality.

**Results:** about, 1,520 patients aged ≥65 years (60.3% male, median age of 76 [IQR 71–83] years) were included. Comorbidities such as hypertension (69.2%), dyslipidaemia (48.6%), cardiovascular diseases (any chronic heart disease in 38.4% and cerebrovascular disease in 12.5%), and chronic lung disease (25.3%) were prevalent, and 49.6% were on ACEI/ARBs. Patients aged 75 years and older suffered more in-hospital complications (respiratory failure, heart failure, renal failure, sepsis) and a significantly higher mortality (18.4 vs. 48.2%, $P < 0.001$), but fewer admissions to intensive care units (11.2 vs. 4.8%). In the overall cohort, multivariable analysis demonstrated age ≥75 (OR 3.54), chronic kidney disease (OR 3.36), dementia (OR 8.06), peripheral oxygen saturation at admission <92% (OR 5.85), severe lymphopenia (<500/mm$^3$) (OR 3.36) and qSOFA (Quick Sequential Organ Failure Assessment Score) >1 (OR 8.31) to be independent predictors of mortality.

**Conclusion:** patients aged ≥65 years hospitalised for COVID-19 had high rates of in-hospital complications and mortality, especially among patients 75 years or older. Age ≥75 years, dementia, peripheral oxygen saturation <92%, severe lymphopenia and qSOFA scale >1 were independent predictors of mortality in this population.


**Keywords:** Coronavirus disease 2019, SARS-CoV-2, older adults, comorbidities

### Key Points

- It is known that COVID-19 is characterized by high morbidity and mortality, particularly in older patients.
- In our study, patients aged 65 years or older had high rates of in-hospital complications and mortality.
- Age ≥75 years, dementia, peripheral saturation of O2 <92%, severe lymphopenia and qSOFA scale >1 were predictors of mortality.

## Introduction

On 11 March 2020, the World Health Organization (WHO) declared the novel coronavirus disease 2019 (COVID-19), a condition caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), as a pandemic [1].

COVID-19 is characterized by poor outcomes and mortality, especially among older patients [2]. In fact, from the beginning of the epidemic, older age has been identified as an important risk factor for disease severity, with increasing rates of mortality across every decade of life [3–6].

This may be a consequence of poorer previous health status, with higher prevalence of pre-existing comorbidities and a higher degree of frailty [7]. Whether worse quality of care in settings where healthcare systems were overwhelmed may also contributed to the observed poor prognosis is unclear. As older patients represent a vulnerable population, comprehensive data are needed in order to improve health care pathways in the context of the COVID-19 pandemic.

Herein, our first objective was to provide a detailed description of clinical characteristics, initial symptoms and management of a cohort of 65 years or older individuals hospitalised for COVID-19. Furthermore, we aimed to present outcomes and to investigate predictors of in-hospital mortality in this highly susceptible population. Finally, we assessed the differences in terms of baseline characteristics, prognosis and treatment among patients 75 years or older.

## Methods

Please see Appendix A2.

## Results

About, 1,520 patients aged ≥65 years were included in the study (Appendix A1g). About, 916 (60.3%) were male and median age was 76 (IQR 71–83) years (Appendix A1h). The most prevalent comorbidities were hypertension (69.2%), dyslipidaemia (48.6%), cardiovascular diseases (any heart disease in 38.4% and cerebrovascular disease in 12.5%) and chronic lung disease (25.3%). In the overall cohort, 49.6% were on ACEI/ARBs and 19.3% on oral anticoagulation. Median Charlson Comorbidity Index (CCI) was 1 (IQR 1–3) and the median duration of hospitalization in those

patients who survived was 8 (IQR 4–12) days. Clinical baseline characteristics are shown in Table 1 (summary) and Appendix A1a.

At admission, blood tests demonstrated elevated C-reactive protein levels in 92.2% of patients, as well as elevated levels of lactate dehydrogenase (79.2%), D-dimer (72.6%), ferritin (61.2%), transaminases (42.7%) and troponin (21.8%). Severe lymphopenia (<500/mm$^3$) was observed in 18.1% of patients.

### In-hospital complications and treatment

About, 10.7% of patients had a qSOFA at admission of 2–3 points. During hospitalization, 369 (24.8%) patients developed renal failure (KDIGO stage 1 acute kidney injury or worse), 902 (60.1%) patients developed respiratory failure, 143 (9.7%) suffered heart failure, 248 (16.7%) suffered sepsis and 342 (23.5%) developed systemic inflammatory response syndrome (SIRS). In addition, 38 patients (2.6%) had an episode of relevant bleeding during hospitalization and 19 (1.3%) an embolic event. Hydroxychloroquine, antibiotics (e.g. Azithromycin) and antiviral drugs were frequently used (82.2, 78.7 and 59.1%, respectively). Almost 80% required oxygen during admission and 6.4% used mechanical ventilation. A detailed description can be found in Table 1.

### Patients aged 75 years or older

A comparison between patients aged 65–74 and ≥75 years in terms of baseline characteristics, baseline medication, symptoms, in-hospital outcomes and therapies is shown in Table 2 (Summary) and Appendix A1b, S2. Patients aged 75 years or older had more comorbidities such as hypertension, chronic kidney disease, chronic cardiac diseases and dementia, with higher CCI (1.4 vs. 2.0 points). Consequently, almost all types of medication were more prevalent at the point of hospital admission. Apart from dyspnoea and fatigue, common presenting symptoms of COVID-19 were less prevalent in the older age group' (e.g. fever 82 vs. 74.2%). Clinical parameters such as peripheral oxygen saturation <92% (35.7 vs. 52.0) and those used for qSOFA calculation were more frequently abnormal at admission.

Almost all in-hospital complications were more frequent in patients older than 75 years (Figure 1). However, admission to ICU was limited to 42 patients (11.2 vs. 4.8%), and invasive mechanical ventilation was used in 4.4% of patients ≥75 years. Other commonly used treatments for COVID-19, such as hydroxychloroquine, antiviral drugs, interferon and tocilizumab were prescribed less frequently to those aged 75 and over.

### Analysis of the primary outcome

All-cause mortality was 541 of 1,520 participants (35.6%). A higher mortality across increasing age subgroups was found, from 11.7% in patients 65–69 years to 54.5% in patients above 80 years (Figure 2). When divided into two subgroups, 65–74 and ≥75 years, mortality was significantly higher in the latter (18.4 vs. 48.2%, $P$ <0.001) (Appendix A1i). The influence of comorbidities in mortality in both groups is shown in Appendix A1j. A clear trend towards worse outcomes with higher CCI scores, especially in patients 75 years and older, was observed. Among patients who died invasive therapies had been used less frequently in those aged over 75 years compared to the younger group, which remained statistically significant even after adjusting for Charlson index (0 or 1 point), dementia and dependency (Appendix A1c).

We investigated those factors associated with higher risk of mortality. Univariate regression analyses are detailed in Appendix A1d. Age ≥75 (OR 3.54, 95% CI 1.76–8.38), chronic kidney disease (3.36, 95% CI 11.00–11.33), dementia (8,06, 95% CI 1.45–44.85), peripheral oxygen saturation < 92% (5.85, 95% CI 2.89–11.84), severe lymphopenia (3.36, 95% CI 1.53–7.38) and qSOFA >1 (8.31, 95% CI 2.29–30.16) were independent predictors of death (Appendix A1e and Table 3).

## Discussion

This is, to the best of our knowledge, one of the largest studies with detailed data focused on older patients with COVID-19 to date. As in previous studies, the main finding was a high risk of in-hospital mortality among these patients.

From the beginning of the epidemic, older age has been associated with worse outcomes. For example, Wu et al., in the Chinese Center for Disease Control and Prevention report of 72,314 cases, found an overall fatality rate of 2.4%, increasing to 8.0% in patients aged 70–79 years and 14.8% in those older than 80 [6]. In Italy, an analysis of the first 2003 deaths from COVID-19 by the Italian National Institute of Health found that the median age of those who died was 80.5 years (IQR 74.3–85.9) with 87.7% being older than 70 years [11]. In a more recent study that included 8,910 patients from Asia, Europe and America, an age greater than 65 years was found to be independently associated with an increased risk of in-hospital death (mortality of 10.0 vs. 4.9% among those ≤65 years of age) [12].

In our cohort of older people with COVID-19, we found an increasing in-hospital mortality across ages, from 11% in patients aged 65–69 to more than 50% in those aged 80 or older. Although this may seem a significantly higher rate of mortality than the previously mentioned studies, asymptomatic patients and those with mild degrees of the disease were not usually hospitalised and thus, they are not represented in our population of study. However, when comparing with reports of hospitalised patients from China, we also find differences in outcomes. For example, from a cohort of 1,099 patients in the first two months of the outbreak, Guan et al. reported 153 patients aged ≥65 with a presence of composite end-point (admission in ICU, mechanical ventilation or death) in 20.9% of them, and death occurring in only 15 patients of the overall cohort. This may be explained

**Table 1**. Baseline characteristics of the overall cohort

| Characteristic | Overall cohort of patients ≥ 65 years (*N*=1,520) |
|---|---|
| Age (years), median [IQR][a] | 76 [71–83] |
| Male sex, *n* (%) | 916/1,520 (60.3) |
| Race, white or Caucasian race, *n* (%) | 1,402/1,520 (92.2) |
| Body mass index (kg/m$^2$), median [IQR][b] | 27.6 [25.1–30.9] |
| Duration of stay (days), median [IQR] | 8 [5–13] |
| Chronic conditions, *n* (%) | |
| **Hypertension** | 1,047/1,514 (69.2) |
| **Dyslipidaemia** | 728/1,499 (48.6) |
| **Diabetes mellitus** | 377/1,435 (26.3) |
| **Obesity** | 267/1,058 (25.2) |
| **Current smoking** | 72/1,520 (4.7) |
| **Chronic kidney disease**[c] | 164/1,440 (11.4) |
| **Chronic lung disease** | 380/1,502 (25.3) |
| **Any heart disease** | 562/1,463 (38.4) |
| **Atrial Fibrillation** | 247/1,518 (16.3) |
| **Cerebrovascular disease** | 185/1,475 (12.5) |
| **Connective tissue disease** | 63/1,471 (4.3) |
| **Liver disease** | 61/1,456 (4.2) |
| **Cancer** | 295/1,464 (20.2) |
| **Parkinsons disease** | 18/1,154 (1.6) |
| **Dementia** | 70/1,154 (6.1) |
| Immunosuppression, *n* (%)[d] | 119/1,325 (9.0) |
| Prior tuberculosis, *n* (%) | 18/1,154 (1.6) |
| Human immunodeficiency virus, *n* (%) | 2/1,154 (0.2) |
| Charlson Comorbidity Index (points), median [IQR] | 1 [0–3]/1,011 |
| Home oxygen therapy, *n* (%) | 75/1,504 (5.0) |
| Preadmission medication, *n* (%)[e] | |
| **ASA** | 336/1,487 (22.6) |
| **Other antiplatelet drug** | 91/1,456 (6.3) |
| **Oral anticoagulation** | 287/1,487 (19.3) |
| **ACEI/ARB's** | 743/1,499 (49.6) |
| **Beta blockers** | 376/1,493 (25.2) |
| Symptoms, *n* (%) | |
| **Asymptomatic** | 67/1,490 (4.5) |
| **Dyspnoea**[f] | 874/1,493 (58.5) |
| **Tachypnoea> 22 breaths per minute** | 450/1,430 (31.5) |
| **Fatigue** | 706/1,448 (48.8) |
| **Anosmia/Hyposmia** | 50/1,376 (3.6) |
| **Altered taste** | 74/1,378 (5.4) |
| **Sore throat** | 136/1,397 (9.7) |
| **Fever** | 1,165/1,503 (77.5) |
| **Cough** | 983/1,486 (66.2) |
| **Vomiting** | 109/1,441 (7.6) |
| **Diarrhoea** | 253/1,440 (17.6) |
| **Arthromyalgia** | 397/1,451 (27.6) |
| qSOFA >1, *n* (%) | 122/1,136 (10.7) |
| X-Ray abnormalities, *n* (%)[g] | 1,206/1,520 (79.4) |
| **Complications during admission, *n* (%)** | |
| Respiratory failure | 902/1,501 (60.1) |
| Heart failure | 143/1,476 (9.7) |
| Acute kidney Injury | 369/1,489 (24.8) |
| Upper respiratory tract infection | 203/1,427 (14.2) |
| Pneumonia | 1,346/1502 (89.6) |
| Sepsis | 248/1,482 (16.7) |
| Systemic inflammatory response syndrome | 342/1,454 (23.5) |
| Any relevant bleeding[h] | 38/1,454 (2.6) |
| Hemoptysis | 36/1,467 (2.5) |
| Embolic event | 19/1,462 (1.3) |
| **Oxygen therapy at the admission, n (%)** | |
| Oxygen during admission | 1,204/1,506 (79.9) |
| High flow nasal cannula | 348/1,480 (23.5) |
| Non-invasive mechanical ventilation | 238/1,472 (15.7) |
| Invasive mechanical ventilation | 92/1,448 (6.4) |
| Prone position | 164/1,454 (11.3) |
| Circulatory support or ECMO | 41/1,447 (2.8) |
| Duration of mechanical ventilation (days), median (IQR) | 8.0 [3.5–13.5] |
| **Other therapies during the admission, n (%)** | |
| Use of glucocorticoids | 403/1,476 (27.3) |
| Use of chloroquine and derivatives | 1,226/1,492 (82.2) |
| Use of antiviral drugs[i] | 899/1,488 (59.1) |
| Use of interferon | 215/1,465 (14.7) |
| Use of tocilizumab | 101/1,466 (6.9) |
| Use of antibiotics | 1141/1,449 (78.7) |
| ACEI/ARB's | 329/1,397 (23.6) |
| **ICU admission, *n* (%)** | **114/1,520 (7.5)** |
| **Death, *n* (%)** | **541/1,520 (35.6)** |

**Abbreviations**: **ACEI** = Angiotensin converting enzyme (ACE) inhibitors; **ARB** = Angiotensin receptors blockers; **ASA** = Acetylsalicylic acid; **ECMO** = Extracorporeal membrane oxygenation; **ICU** = Intensive Care Unit; **qSOFA** = Quick Sequential Organ Failure Assessment Score. [a]Detailed distribution of patients according to age is shown in Appendix A1g. [b]The body-mass index is the weight in kilograms divided by the square of the height in meters. [c]Creatinine clearance < 30 mL/min. [d]Immunosuppressive therapy for psoriasis arthritis, lung transplantation, kidney transplantation or systemic lupus erythematosus; oncological disease such as breast cancer, prostate cancer, myelodysplastic syndrome or gammopathy; glucocorticoid therapy caused by COPD; dialysis; HIV or hepatitis C. [e]Other pre-medications are listed in Appendix A1b. [f]Severity of dyspnoea is described in Appendix A1b. [g]Detailed data are listed in in Appendix A1b. [h]Rectorrhagia, haematuria, epistaxis, and popliteal aneurysm bleeding with relevant decreased haemoglobin> 2 mg/l. [i]Lopinavir or/and Ritonavir were the most commonly used antivirals.

**Table 2**. Characteristics of patients aged 65–74 as compared to patients aged ≥75*

| Characteristic | 65–74 *N*= 642 | ≥75 *N*= 878 | P value |
|---|---|---|---|
| Age (years), mean ± SD | 69.9 ± 2.8 | 83.2 ± 6.1 | <**0.001** |
| Male sex, *n* (%) | 387/642 (60.3) | 529/878 (60.3) | 0.99 |
| Duration of stay (days), mean ± SD | 9.4 ± 7.3 | 8.6 ± 6.9 | **0.05** |
| Chronic conditions, *n* (%) | | | |
| **Hypertension** | 398/639 (62.3) | 649/875 (74.2) | <**0.001** |
| **Dyslipidaemia** | 294/634 (46.4) | 434/865 (50.2) | 0.15 |
| **Diabetes mellitus** | 150/609 (24.6) | 227/826 (27.5) | 0.26 |
| **Obesity** | 132/447 (29.5) | 135/611 (22.1) | <**0.001** |
| **Chronic kidney disease** | 47/616 (7.6) | 117/824 (14.2) | <**0.001** |
| **Chronic lung disease** | 150/637 (23.5) | 230/865 (26.6) | 0.18 |
| **Any heart disease** | 156/632 (24.7) | 406/858 (47.3) | <**0.001** |
| **Cerebrovascular disease** | 46/627 (7.3) | 139/848 (16.4) | <**0.001** |
| **Parkinsons disease** | 2/513 (0.4) | 16/641 (2.5) | **0.01** |
| **Dementia** | 10/513 (1.9) | 60/641 (9.4) | <**0.001** |
| Charlson Comorbidity Index | 1.4 ± 1.7 | 2.0 ± 1.9 | <**0.001** |
| Any dependency level | 36/633 (5.7) | 272/861 (31.6) | <**0.001** |
| Home oxygen therapy, *n* (%) | 20/638 (3.1) | 55/866 (6.4) | **0.01** |
| Preadmission medication, *n* (%) | | | |
| **ASA** | 123/632 (19.5) | 214/856 (25) | **0.01** |
| **Other antiplatelet drugs** | 22/623 (3.5) | 69/834 (8.3) | <**0.001** |
| **Oral anticoagulation** | 68/631 (10.8) | 219/857 (25.6) | <**0.001** |
| **ACEI** | 283/635 (44.6) | 461/865 (53.3) | **0.001** |
| **Beta blockers** | 121/634 (19.1) | 256/860 (29.8) | **0.001** |
| **Beta agonist inhalation therapy** | 74/636 (11.6) | 138/849 (16.3) | **0.01** |
| **Glucocorticoids inhalation therapy** | 62/634 (9.8) | 118/854 (13.8) | **0.02** |
| Symptoms, *n* (%) | | | |
| **Dyspnoea** | 374/635 (58.9) | 500/858 (58.3) | 0.89 |
| **Fatigue** | 303/623 (48.6) | 403/825 (48.8) | 0.93 |
| **Fever** | 523/638 (82.0) | 642/865 (74.2) | <**0.001** |
| **Cough** | 437/632 (69.1) | 546/854 (63.9) | **0.04** |
| **Diarrhoea** | 136/610 (22.3) | 117/830 (14.1) | <**0.001** |
| **Arthromyalgia** | 202/622 (32.5) | 195/830 (23.5) | <**0.001** |
| Clinical parameters, *n* (%) | | | |
| **Peripheral oxygen saturation <92%** | 223/625 (35.7) | 445/856 (52.0) | <**0.001** |
| qSOFA score >1, n (%) | 29/500 (5.8) | 93/636 (14.6) | <**0.001** |
| Laboratory parameters, *n* (%) | | | |
| **Elevated D-dimer** | 388/559 (69.4) | 535/712 (75.1) | **0.02** |
| **Elevated troponin I** | 48/276 (17.4) | 102/413 (24.7) | **0.02** |
| **Severe Lymphopenia (<500/ml)** | 84/600 (14.0) | 175/827 (21.2) | **0.001** |
| X-ray abnormalities | 526/574 (91.6) | 680/806 (84.4) | <**0.001** |
| Complications during admission | | | |
| **Respiratory failure** | 329/636 (51.7) | 573/865 (66.2) | <**0.001** |
| **Heart failure** | 33/626 (5.3) | 110/850 (12.9) | <**0.001** |
| **Acute kidney injury** | 118/634 (18.6) | 251/855 (29.4) | <**0.001** |
| **Pneumonia** | 591/641 (92.2) | 755/861 (87.7) | **0.01** |
| **Sepsis** | 82/632 (13) | 166/850 (19.5) | **0.001** |
| **SIRS** | 134/628 (21.3) | 208/826 (25.2) | 0.09 |
| Oxygen therapy, *n* (%) | | | |
| **Oxygen, any** | 480/635 (75.6) | 724/871 (83.1) | <**0.001** |
| **High flow nasal cannula** | 121/625 (19.4) | 227/855 (26.5) | **0.001** |
| **Non-invasive mechanical ventilation** | 102/623 (16.4) | 136/849 (16.0) | 0.86 |
| **Invasive mechanical ventilation** | 56/621 (9) | 36/827 (4.4) | <**0.001** |
| **Prone position** | 83/615 (13.5) | 81/839 (9.7) | **0.02** |
| **Circulatory support or ECMO** | 27/620 (4.4) | 14/827 (1.7) | **0.01** |
| Other therapies during the Admission, n (%) | | | |
| **Use of Glucocorticoids** | 166/627 (26.5) | 237/849 (27.9) | 0.54 |
| **Use of chloroquine and derivatives** | 559/629 (88.9) | 667/863 (77.3) | <**0.001** |
| **Use of antiviral drugs** | 437/627 (69.7) | 462/861 (53.7) | <**0.001** |
| **Use of interferon** | 105/621 (16.9) | 110/844 (13.0) | **0.04** |
| **Use of tocilizumab** | 60/622 (9.6) | 41/844 (4.9) | <**0.001** |
| **Use of antibiotics** | 479/610 (78.5) | 662/839 (78.9) | 0.86 |
| ICU admission, *n* (%) | 72/642 (11.2) | 42/878 (4.8) | <**0.001** |
| Death, *n* (%) | 118/642 (18.4) | 423/878 (48.2) | <**0.001** |

**Abbreviations**: **ACEI** = Angiotensin converting enzyme (ACE) inhibitors; **ARB** = Angiotensin receptors blockers; **ASA** = Acetylsalicylic acid; **ECMO** = Extracorporeal membrane oxygenation; **ICU** = Intensive Care Unit; **qSOFA** = Quick Sequential Organ Failure Assessment Score; **SIRS** = Systemic Inflammatory Response Syndrome. *Extensive data are listed in Appendix A3.

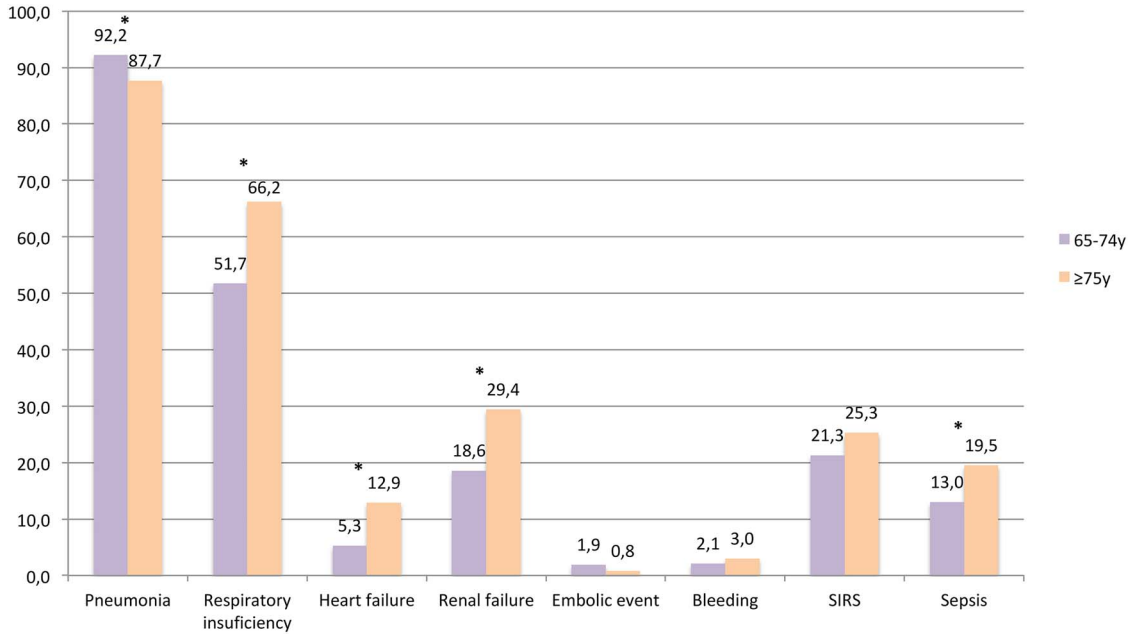


**Figure 1**. Percentage of in-hospital complications in patients aged 65–74 and ≥75 years. *X* axis = type of complication; *Y* axis = percentage (%). *$P$ <0.05.

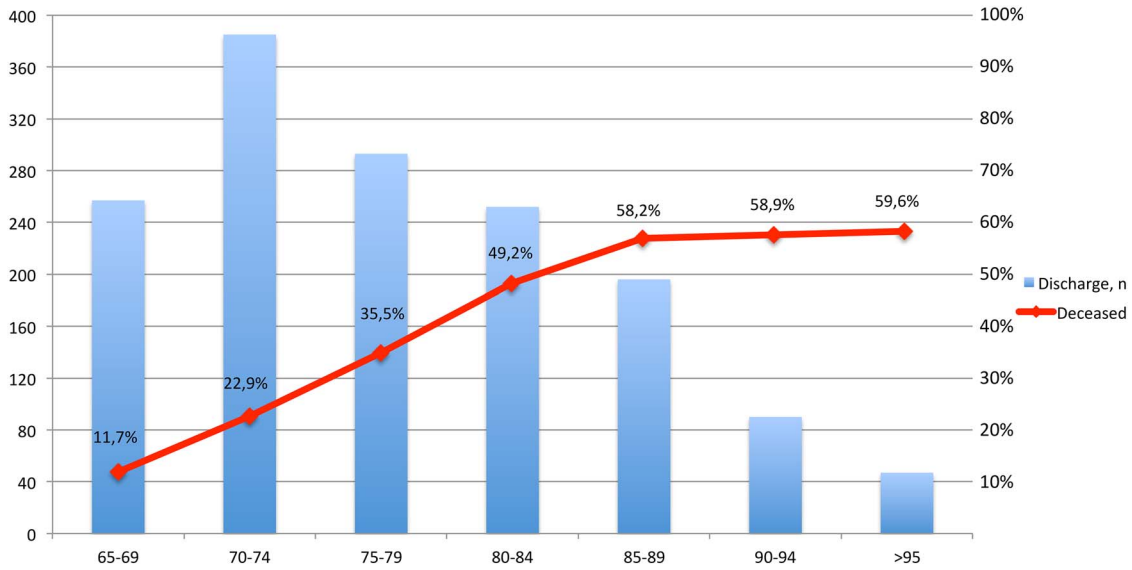


**Figure 2**. Number of patients aged ≥65 years hospitalised for COVID-19 (blue boxes) and percentage of deaths (red dots) according to age.

by younger age of patients included (median age 47 years, with only 15.1% of patients older than 65 years) [4]. A younger age in their overall population or a lower rate of older patients hospitalised in their hospitals may be behind these low percentages of older people. Supporting our belief of a higher mortality than previously reported, McMichael et al. have recently published a rate of 33% of deaths in infected residents of a long-term care facility in Washington, USA [13].

The presence of a higher number of comorbidities and a worse immune response towards the infection may be related to older patients' susceptibility [14]. As in previous studies, we found a high prevalence of comorbidities within these patients admitted to hospital for COVID-19. Previous conditions such as cardiovascular diseases, diabetes mellitus, hypertension, chronic lung diseases, obesity, cancer and chronic kidney disease have been associated with severe illness and mortality [5,6,12,15–17]. In our study, chronic kidney disease (eGFR<30 mL/min/1.73m$^2$) was found to be an independent risk factor of mortality, with an OR 3.36. Kidney disease has been already described as a risk factor for mortality in COVID-19 [18]. Of note, SARS-Cov-2

**Table 3**. Summary of predictors for all cause in-hospital mortality*

| | Multivariable analysis | | |
|---|---|---|---|
| | OR | 95%CI | *P*-value |
| Age≥ 75 | 3.54 | 1.76–8.38 | **<0.001** |
| Chronic kidney disease | 3.36 | 1.00–11.33 | 0.05 |
| Dementia | 8.06 | 1.45–44.85 | **0.017** |
| Peripheral oxygen saturation < 92% | 5.85 | 2.89–11.84 | **<0.001** |
| Severe lymphopenia (<500/mm3) | 3.36 | 1.53–7.38 | **0.003** |
| qSOFA >1 | 8.31 | 2.29–30.16 | **0.001** |

qSOFA = Quick Sequential Organ Failure Assessment Score. *A complete description of variables included in the model is shown in Appendix A1e.

may have itself direct cytopathic effects on kidney tissue [3], entering kidney cells through an angiotensin converting enzyme (ACE)-2-dependent pathway. In addition, immune-mediated damage related to deposition of virus-induced immune complexes has been reported [19]. These facts may worsen function of previously damaged kidneys.

Importantly, this is one of the few studies to associate dementia with worse outcomes (OR 8.06) [20]. Globally, more than 50 million people have dementia [21] and several organizations have recently released recommendations on these patients during the outbreak [22]. We postulate that this higher risk of in-hospital death may be explained by several factors: firstly, a worse baseline health status; secondly, delayed access to hospitals, sometimes in more advanced stages of the disease due to their inability to express some initial symptoms; finally, the difficulties faced by hospital facilities in maintaining quality of care for this very dependent group of patients where isolation, PPE and health system overload are present. Furthermore, it has been recently hypothesized that the presence of ApoE e4e4 allele increases risks of severe COVID-19 infection, independent of pre-existing dementia, cardiovascular disease and type-2 diabetes [20]. It is noteworthy that some prevention strategies have been specifically developed for patients with dementia in dedicated institutions [23].

A very low level of lymphocytes was another independent predictor. It is known that the lymphocyte count decreases in COVID-19 patients [24, 25]. Potential mechanisms may be the lymphocytes death or dysfunction caused directly by the virus or indirectly through inflammatory cytokines or metabolic molecules [26]. In our study, other important predictors of mortality were a qSOFA scale more than 1 point and a peripheral oxygen saturation less than 92% at admission, parameters which reflect a more severe degree of the disease on arrival to the emergency room.

Interestingly, patients 75 years and older were less frequently admitted to ICUs and received less therapies commonly used for COVID-19 treatment. Lian et al., in one of the largest studies evaluating older patients' characteristics to date, reported higher rates of ICU admission (9.56 vs. 1.38%) and methylprednisolone application (28.68 vs. 9.36%) when compared with younger patients (cut-off point 60 years) [27]. However, they did not make any distinction among ages above 60 years. Our finding of a trend towards less invasive therapies in the oldest subgroup led us to undertake a further subgroup analysis (Appendix A1c), comparing deceased patients younger and older than 75 years without significant comorbidities (Charlson Comorbidity Index of 0 or 1, without any degree of dementia or dependency). We found that there is still a subset of 'previously healthy patients' who were deceased without having been admitted to any ICU or without having undergone more advanced techniques, such as mechanical ventilation, circulatory support or the use of drugs such as tocilizumab. For this reason, we assume that age may had been the only limitation for them. This is consistent with the Italian guidelines that recommended, in resource-limited circumstances, consideration of prognosis—how long the patient is likely to live if treated— potentially assigning a higher priority for intensive care access to younger patients with severe illness than to older patients [28,29]. However, several societies have stated that advanced age should not by itself be a criterion for excluding patients from some treatments or specialized hospital units [14,30,31]. For example, NICE guidelines recommend the use of Clinical Frailty Scale (CFS) in patients aged 65 years and older as a guidance for the decision [32], although it may also have its important limitations [33]. Furthermore, some authors consider that, for the healthcare systems in many countries, it may be crucial to reconfigure services to cope with demand [34].

Other interesting findings from our study are the widespread use of unevidenced treatments such us hydroxychloroquine, azithromycin and antivirals; and the finding of different patterns of initial symptoms in older patients, with low levels of some of the usually considered 'core features' such as anosmia. This fact should be taken into account when evaluating older patients with suspicion of COVID-19.

To conclude, long-term care facilities deserve special attention in this COVID-19 pandemic, due to their vulnerability to respiratory disease outbreaks [35, 36]. It is known that they are the origin of a very high number of new cases, and a high mortality has been observed [14]. Given that vaccines and antiviral medications are not currently available for Covid-19, other prevention strategies should be enhanced. Among them, screening and restricted access for visitors, screening of health care personnel, including measurement of body temperature, social distancing, including restricting resident movement, staff hands-on

training and education on infection prevention and PPE use, should be applied [13,14,37,38].

### Limitations

There are some limitations to acknowledge regarding our study. Firstly, it is limited by its observational design: disparities in treatment and criteria of admission to ICU may be found among countries, centres and pandemic timing. Besides, some previous conditions and symptoms such as dementia or altered taste may be underreported, as data depended on electronic medical records. Secondly, the sample size is limited, since it only includes hospitalised patients. Thirdly, the original design of the study did not include data about frailty, as well as presentation with delirium nor other parameters that may have been used in prognostic tools such as NEWS-2 or CURB-65. Finally, although this cohort was collected in a prospective manner, the results reported in this study are based on a post hoc analysis and should be regarded as hypothesis generating. However, our study provides a 'real-world' observation on the management and prognosis of these patients and interesting conclusions can be derived.

## Conclusion

In our study, patients aged 65 years or older hospitalised for COVID-19 had high rates of in-hospital complications and mortality, especially among patients older than 75. Age ≥75 years, dementia, peripheral oxygen saturation at admission <92%, severe lymphopenia and qSOFA scale >1 were independent predictors of mortality in this population. Our data support other studies' findings that older people are more vulnerable to COVID-19, and preventive measures should be enhanced among them.

**Supplementary Data:** Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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Please see Appendix 4 for a full list of references.

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