RESEARCH PAPER

Clinical presentation and outcome across age categories among patients with COVID-19 admitted to a Spanish Emergency Department

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Key summary points

Aim According to age, there are differences in the clinical profile, presentation, management, and short-term outcomes of patients with COVID-19 admitted to the Emergency Department.

Findings A statistically significant association was found between demographic data, comorbidities, clinical, radiographic, analytical, and therapeutic variables and short-term results according to age-dependent categories. Age was a prognostic factor for hospital admission and in-hospital and 30-day mortality, and was associated with not being admitted to intensive care.

Message Clinical presentation, management, and short-term outcomes differ according to age among patients with COVID-19 admitted to the Emergency Department.

Abstract

Purpose To determine the differences by age-dependent categories in the clinical profile, presentation, management, and short-term outcomes of patients with laboratory-confirmed COVID-19 admitted to a Spanish Emergency Department (ED).

Methods Secondary analysis of COVID-19_URG-HCSC registry. We included all consecutive patients with laboratory-confirmed COVID-19 admitted to the ED of the University Hospital Clinico San Carlos (Madrid, Spain). The population was divided into six age groups. Demographic, baseline and acute clinical data, and in-hospital and 30-day outcomes were collected.

Results 1379 confirmed COVID-19 cases (mean age 62 (SD 18) years old; 53.5% male) were included (18.1% < 45 years; 17.8% 45–54 years; 17.9% 55–64 years; 17.2% 65–74 years; 17.0% 75–84 years; and 11.9% ≥ 85 years). A statistically significant association was found between demographic, comorbidity, clinical, radiographic, analytical, and therapeutic variables and short-term results according to age-dependent categories. There were less COVID-specific symptoms and more atypical symptoms among older people. Age was a prognostic factor for hospital admission (aOR = 1.04; 95% CI 1.02–1.05) and in-hospital (aOR = 1.08; 95% CI 1.05–1.10) and 30-day mortality (aOR = 1.07; 95% CI 1.04–1.09), and was associated with not being admitted to intensive care (aOR = 0.95; 95% CI 0.93–0.98).

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Conclusions Older age is associated with less COVID-specific symptoms and more atypical symptoms, and poor short-term outcomes. Age has independent prognostic value and may help in shared decision-making in patients with confirmed COVID-19 infection.

Keywords Age · Older · COVID-19 · Emergency department

Introduction

Since December 2019, when the first case of coronavirus disease-2019 (COVID-19) was reported in Wuhan (Hubei, China), the virus has spread worldwide, causing a global pandemic, which has become an international public health emergency [1]. Spain has been one of the countries most affected in the world, with the region of Madrid presenting some of the highest case and mortality rates [2]. Spain has an increasingly ageing society [3]. A high frequency of deaths by COVID-19 has been documented in older people [2, 4, 5], with the mortality rate by COVID-19 increasing with age from 5% in subjects between 60 and 69 years of age to 14.3% in those between 70 and 79 years and up to 21.3% in individuals over 80 years old [2].

Older people are characterised by physiological ageing changes, multiple age-related comorbid conditions, and polypharmacy [6]. These circumstances facilitate the presentation of nonspecific and atypical clinical manifestations [4, 7]. The immune system of older adults undergoes several age-related changes, collectively termed immune senescence, involving many cellular and molecular elements of both innate and adaptive immune systems, making this group more vulnerable to infectious diseases [8]. In addition, certain comorbidities such as cardiovascular risk factors, and chronic diseases and cancer have been associated with poor outcomes [9]. All of these factors can contribute to poor health outcomes [4, 7, 8].

The scientific community is demanding specific information about older people and the establishment of their needs [10]. Unfortunately, the clinical characteristics of COVID-19 infection are little known in this age group. Furthermore, there is not enough evidence about the clinical profile and results in patients admitted to Emergency Departments (EDs). So far, there is little information on age-based clinical features, medical management, and short-term outcomes of COVID-19 in the ED. The objective of the present study was to determine whether there are differences in the clinical profile, presentation, management, and short-term outcomes of patients with laboratory-confirmed COVID-19 admitted to a Spanish ED according to age-dependent categories.

Methods

Study design

This is a secondary analysis of the COVID-19_URG-HCSC registry. This registry is a retrospective, observational cohort study, including all suspected COVID-19 cases in the ED of the University Hospital Clinico San Carlos (HCSC).

The HCSC is an urban public tertiary university hospital in Madrid with a reference area of 400,000 inhabitants. The ED of the HCSC attends 140,000 cases per year, with independent Paediatrics, Traumatology, Gynaecology-Obstetrics, and Psychiatry areas. Although a telephone consultation system attended by emergency medical services (EMS) was specifically created during the pandemic and every citizen in our region is assigned a general practitioner (GP), the ED was opened to everyone regardless of the severity of symptoms or previous contact with GPs or the EMS.

The COVID-19_URG-HCSC registry is part of the clinical database that was specifically created for the COVID-19 pandemic (BDCLIN_HCSC_COVID-19). The BDCLIN_HCSC_COVID-19 is a secure institutional electronic data capture system and repository, which includes the sociodemographic, clinical, diagnostic test, and therapeutic and clinical follow-up data of all the COVID-19 cases handled in the HCSC. Since the 28th of February 2020, the information is being sequentially and additively incorporated from several clinical and administrative sources and will continue to be incorporated throughout the pandemic.

Patient selection

For the present study, laboratory-confirmed COVID-19 cases admitted to the ED from 28 February 2020 to 31 March 2020 were included. Diagnosis was made by the detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR) in nasopharynx and oropharynx samples. In cases, in which the RT-PCR was repeated, because the result was non-conclusive or a false-negative result was suspected, the last result of the diagnostic test performed during the study period was selected. The study population was divided into six age groups: group 1: 18–44 years old; group 2: 45–54 years old; group 3: 55–64 years old; group 4: 65–74 years old; group 5: 75–84 years old; and group 6: ≥ 85 years old.

Clinical assessment, data collection and follow-up

Clinical assessment at the ED included medical history, physical examination, chest radiography, laboratory test, and RT-PCR if available. The criteria for requesting RT-PCR were determined by instructions from the Spanish

Ministry of Health [11], which varied along the study period. Until March 11th, when Madrid was recognized as an area with community transmission, emergency medicine physicians could only order tests for patients admitted for severe viral pneumonia or those who met epidemiological criteria. After this date, SARS-CoV-2 testing was always requested in suspected, more vulnerable, institutionalized, or hospitalized cases. A semi-structured medical record for clinical practice was designed as a modified version of the WHO/International Severe Acute Respiratory and Emerging Infection Consortium Rapid Case Report Form [12] and included clinical symptoms and signs, radiological, laboratory, and COVID-19 treatments. The data of the COVID-19_URG-HCSC registry were entered from medical records by eight investigators using REDCap (Research Electronic Data Capture) (Table in Online Supplementary Material). All the investigators involved in the data collection had been previously trained in information collection. To establish the quality and accuracy of each data included, all the information was checked by a trained researcher. This system ensured the quality of the information included in this study. Patient follow-up was performed 30 days after the index episode by accessing the regional administrative database and hospital and primary care electronic medical records or by telephone contact when necessary to know the vital status of the patients. Patient management was left to the discretion of the attending physician. This guideline was based on recommendations by the Spanish Government and Scientific Societies [13].

Study variables

Data were collected on sociodemographic (3 variables), medical history (14 variables), chronic treatment (4 variables), baseline functional status (1 variable), clinical symptoms and signs (20 variables), radiological (4 variables), laboratory (17 variables), and COVID-19 treatments (7 variables). The outcomes were hospital admission, high-flow oxygen requirement, intensive-care unit (ICU) admission, and in-hospital and 30-day all-cause mortality.

Statistical analysis

Continuous variables are presented as mean (standard deviation [SD]) or median (interquartile range [IQR]), as appropriate and categorical variables are expressed as numbers and percentages. For the present study, the population was divided into six groups sorted by age-dependent categories. Comparisons among groups were made using the Spearman correlation coefficient for continuous variables and the Chi-square test (or Fisher's exact test when more than

25% of the expected frequencies were < 5) was used for categorical variables. P values for linear trend were estimated. Subgroup analysis for clinical and laboratory variables was made. The reference group in the model was the youngest patient group (18–44 years). 30-day cumulative mortality plots stratified by age-dependent groups were plotted using the Kaplan–Meier method, and univariable associations were compared using the log-rank test. Follow-up started at the time of the ED arrival. Outcomes for the different age groups were compared using multivariable logistic regression. Measures of association were expressed as odds ratio (OR), with a 95% confidence interval (CI), adjusted for sex and co-variables on the basis of clinical interest and relevant prior findings in the literature clinically. Missing values were replaced using the multiple imputation technique, generating five datasets with no missing values for the variables included in the adjustment. Statistically significant differences were considered as a two-side P value less than 0.05 or if the OR 95% CI excluded 1. The sample size was not calculated as this was an exploratory study. Data analysis was performed using SPSS software, version 24.00 (IBM, New Castle, NY, USA) and STATA version 15.1 (Stata Corp, College Station, TX, USA). Some figures were plotted using R statistical software (R foundation for Statistical Computing, Vienna, Austria).

The COVID-19-URG-HCSC registry was developed following the ethical principles of the Declaration of Helsinki for medical research in humans. The protocol and waiver of the need for obtaining informed consent were approved by the HCSC Research Ethics Committee (Cl 20/338-E).

Results

Out of a total of 2193 patients with suspected COVID-19 admitted to the ED, 1379 laboratory-confirmed cases were included in the analysis, thereby excluding 814 (37.1%) subjects, because diagnosis had not been confirmed by RT-PCR (363 cases with negative RT-PCR, 19 cases with non-conclusive RT-PCR, and 432 cases in whom RT-PCR was not performed) (Fig. 1). Diagnostic tests were more frequently performed as age increased (Fig. 1 in Online Supplementary Material).

Characteristics of the study subjects

The median age of the 1379 patients was 63 (IQR 48–77) years and 738 (53.5%) were male; 250 (18.1%) were < 45 years old, 246 (17.8%) 45–54 years, 247 (17.9%) 55–64 years, 237 (17.2%) 65–74 years, 235 (17.0%) 75–84 years, and 164 (11.9%) were 85 years of age or older. The most common comorbidities were hypertension (40.5%), dyslipidaemia (37.9%), and diabetes mellitus
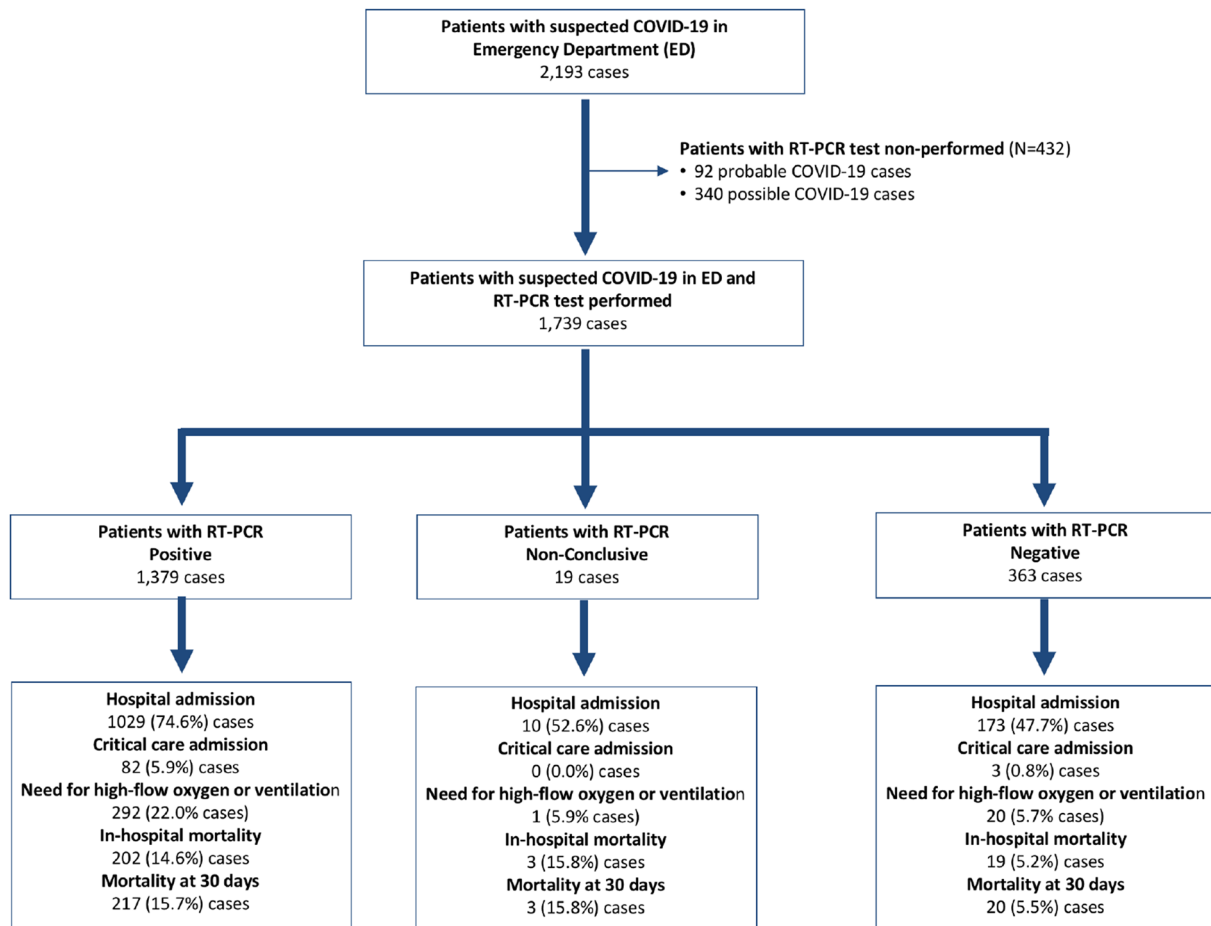
Fig. 1 Flowchart of patient inclusion

(9.2%). Among the population cohort, 80.0% had subjective fever, 71.1% cough, and 47.74% dyspnoea. Regarding the vital sign at arrival to the ED, 33.7% had fever (≥ 38 °C) and 23.6% hypoxemia (O2 saturation < 92%). Chest X-ray was performed in 1348 patients, 69.8% of whom showed abnormal results. The most common treatment for COVID-19 was hydroxychloroquine (71.3%) following by antibiotics (63.7%), lopinavir/ritonavir (45.6%), and corticosteroids (19.9%) (Tables 1, 2 and 3).

Comparison of patient characteristics by age-dependent categories

Regarding the relationship between cardiovascular risk factors and age groups, there was a higher frequency of hypertension ($P < 0.001$), dyslipidaemia ($P < 0.001$), and diabetes mellitus ($P < 0.001$) with increasing age. Conversely, there was a lower percentage of current smokers ($P < 0.001$) (Table 1).

With respect to comorbidities, there was an increase in cancer and all degenerative and chronic diseases with age, except for HIV. Simultaneously, there was a higher frequency of treatments with angiotensin-converting enzyme inhibitors (ACEs)/angiotensin II receptor blockers (ARBs) ($P < 0.001$), anticoagulation ($P < 0.001$), antiplatelet ($P < 0.001$), and immunosuppressive agents ($P < 0.001$) with increasing age (Table 1).

Statistically significant differences by age-dependent categories were also found in terms of clinical symptoms and signs. Older subjects presented fewer core COVID-19 symptoms and more typical geriatric complaints. The population aged 65 and older showed a higher percentage of patients with confusion ($P < 0.001$), asthenia ($P = 0.033$), and pre/syncope ($P < 0.001$) (Table 2).

There was an indirect relationship between age and oxygen saturation ($P < 0.001$) and body temperature ($P = 0.002$) and a direct relationship between age and systolic blood pressure ($P = 0.043$) at arrival to the ED (Table 2).

Table 1 Socio-demographic and medical history data of the study population by age-dependent categories

	Patients N=1379 N (%)	18–44 years, N=250 n (%)	45–54 years, N=246 n (%)	55–64 years, N=247 n (%)	65–74 years, N=237 n (%)	75–84 years, N=235 n (%)	≥85 years, N=164 n (%)	P value
Socio-demographic data								
Male gender	739 (53.6)	136 (54.4)	133 (54.1)	124 (50.2)	140 (59.1)	125 (53.2)	80 (48.8)	**0.545**
Living in nursing home	33 (2.4)	1 (0.4)	2 (0.8)	1 (0.4)	4 (1.7)	6 (2.6)	19 (11.7)	**< 0.001**
Medical history								
Current smoking	61 (4.4)	9 (3.6)	9 (3.7)	13 (5.3)	21 (8.9)	6 (2.6)	3 (1.8)	**< 0.001**
Hypertension	559 (40.5)	6 (2.4)	41 (16.7)	78 (31.6)	148 (62.4)	167 (71.1)	119 (72.6)	**< 0.001**
Diabetes mellitus	265 (19.2)	7 (2.8)	17 (6.9)	35 (14.2)	73 (30.8)	80 (34.0)	53 (32.3)	**< 0.001**
Dyslipidemia	523 (37.9)	8 (3.2)	38 (15.4)	96 (38.9)	146 (61.6)	147 (62.6)	88 (53.7)	**< 0.001**
Obesity	131 (9.5)	20 (8.0)	25 (10.2)	26 (10.5)	28 (11.8)	24 (10.2)	8 (4.9)	**0.664**
Chronic respiratory disease	239 (17.3)	17 (6.8)	24 (9.8)	30 (12.1)	59 (24.9)	62 (26.4)	47 (28.7)	**< 0.001**
Heart disease	237 (17.2)	6 (2.4)	7 (2.8)	19 (7.7)	49 (20.7)	70 (29.8)	86 (52.4)	**< 0.001**
Peripheral artery disease	36 (2.6)	0 (0.0)	0 (0.0)	3 (1.2)	7 (3.0)	13 (5.5)	13 (7.9)	**< 0.001**
Cerebrovascular disease	58 (4.2)	0 (0.0)	1 (0.4)	3 (1.2)	15 (6.3)	24 (10.2)	15 (9.1)	**< 0.001**
Dementia	67 (4.9)	0 (0.0)	1 (0.4)	1 (0.4)	8 (3.4)	18 (7.7)	39 (23.8)	**< 0.001**
Chronic renal disease	109 (7.9)	1 (0.4)	7 (2.8)	11 (4.5)	29 (12.2)	39 (16.6)	22 (13.4)	**< 0.001**
Liver disease	43 (3.1)	0 (0.0)	8 (3.3)	11 (4.5)	10 (4.2)	7 (3.0)	7 (4.3)	**0.031**
Cancer	130 (9.4)	4 (1.6)	13 (5.3)	19 (7.7)	30 (12.7)	41 (17.4)	23 (14.0)	**< 0.001**
HIV	16 (1.2)	4 (1.6)	5 (2.0)	4 (1.6)	3 (1.3)	0 (0.0)	0 (0.0)	**0.020**
Connective tissue disease	20 (1.4)	0 (0.0)	5 (2.0)	3 (1.2)	3 (0.8)	4 (1.7)	6 (3.7)	**0.012**
Baseline functional status								
Independent BADL	1220 (91.4)	246 (98.8)	235 (98.3)	237 (97.9)	217 (94.3)	198 (87.2)	87 (58.8)	**< 0.001**
Partially dependent BADL	64 (4.8)	0 (0.0)	2 (0.8)	5 (2.1)	8 (3.5)	17 (7.5)	32 (21.6)	
Total dependent BADL	51 (3.8)	3 (1.2)	2 (0.8)	0 (0.0)	5 (2.2)	12 (5.3)	29 (19.6)	
Chronic treatment at home								
ACEis / ARBs	440 (31.9)	6 (2.4)	30 (12.2)	63 (25.5)	111 (46.8)	138 (58.7)	92 (56.1)	**< 0.001**
Anticoagulation	124 (9.0)	1 (0.4)	2 (0.8)	9 (3.6)	20 (8.4)	43 (18.3)	49 (29.9)	**< 0.001**
Antiplatelet agent	208 (15.1)	1 (0.4)	10 (4.1)	20 (8.1)	52 (21.9)	66 (28.1)	59 (36.0)	**< 0.001**
Immunosuppressive treatment	95 (6.9)	3 (1.2)	13 (5.3)	16 (6.5)	22 (9.3)	24 (10.2)	17 (10.4)	**< 0.001**

P value for lineal trend. Numbers in bold mean value $P < 0.05$

HIV human immunodeficiency virus, BADL basic activities of daily living, ACE angiotensin-converting enzyme inhibitors, ARBs angiotensin II receptor blockers

Table 2 Clinical data at presentation of the study population by age-dependent categories

	Patients N = 1379 n (%)	18–44 years, N = 250 n (%)	45–54 years, N = 246 n (%)	55–64 years, N = 247 n (%)	65–74 years, N = 237 n (%)	75–84 years, N = 235 n (%)	>= 85 years, N = 164 n (%)	P value
Acute episode clinical data								
Time of evolution, days [median (IQR)]	7 (3–9)	3 (6–7)	4 (7–9)	4 (7–9)	3 (7–10)	4 (7–8)	2.5 (4–7)	0.657
Cough	981 (71.1)	196 (78.1)	170 (69.1)	189 (76.5)	168 (70.9)	158 (67.2)	100 (61.0)	**< 0.001**
Fever	1104 (80.0)	208 (83.2)	204 (82.9)	207 (83.8)	193 (81.4)	180 (76.6)	111 (67.7)	**< 0.001**
Dyspnoea	653 (47.3)	120 (47.8)	121 (49.2)	123 (49.8)	115 (48.5)	100 (42.6)	74 (45.1)	0.222
Chest pain	158 (11.4)	38 (15.1)	36 (14.6)	34 (13.8)	31 (13.1)	11 (4.7)	8 (4.9)	**< 0.001**
Diarrhoea	275 (19.9)	42 (16.8)	56 (22.8)	62 (25.1)	59 (24.9)	39 (16.6)	16 (9.8)	0.056
Nausea and vomiting	137 (9.9)	35 (13.9)	22 (8.9)	27 (10.9)	30 (12.7)	18 (7.7)	5 (3.0)	**0.002**
Headache	148 (10.7)	41 (16.3)	41 (16.7)	32 (13.0)	17 (7.2)	9 (3.8)	8 (4.9)	**< 0.001**
Confusion	38 (2.8)	0 (0.0)	1 (0.4)	1 (0.4)	8 (3.4)	12 (5.1)	16 (9.8)	**< 0.001**
Anosmia	57 (4.1)	15 (6.0)	23 (9.3)	10 (4.0)	8 (3.4)	0 (0.0)	1 (0.6)	**< 0.001**
Dysgeusia	59 (4.3)	12 (4.8)	18 (7.3)	15 (6.1)	11 (4.6)	2 (0.9)	1 (0.6)	**< 0.001**
Myalgia	313 (22.7)	73 (29.2)	72 (29.3)	74 (30.0)	40 (16.9)	35 (14.9)	18 (11.0)	**< 0.001**
Asthenia	449 (32.5)	63 (25.2)	79 (32.1)	82 (33.2)	90 (38.0)	82 (34.9)	53 (32.3)	**0.033**
Sore throat	89 (6.4)	27 (10.8)	19 (7.7)	18 (7.3)	9 (3.8)	12 (5.1)	4 (2.4)	**< 0.001**
Rhinorrhoea	27 (2.0)	12 (4.8)	7 (2.8)	4 (1.6)	0 (0.0)	1 (0.4)	3 (1.8)	**0.001**
Skin lesions	4 (0.3)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0.484
Presyncope or syncope	68 (4.9)	0 (0.0)	11 (4.5)	7 (2.8)	14 (5.9)	20 (8.5)	16 (9.8)	**< 0.001**
Physical data								
Oxygen saturation, % [mean (SD)]	94 (6.6)	97 (3.1)	96 (5.7)	94 (6.2)	93 (6.5)	91 (7.8)	91 (7.4)	**< 0.001**
Body temperature, °C [mean (SD)]	37.5 (2.9)	37.7 (4.2)	37.4 (1.0)	37.7 (4.0)	37.3 (0.9)	37.5 (3.4)	37.1 (0.7)	**0.002**
SBP, mmHg [mean (SD)]	130 (20.8)	125 (17.8)	129 (18.2)	129 (19.1)	132 (19.9)	128 (22.1)	134 (24.8)	**0.043**

P value for lineal trend. Numbers in bold mean value *P* < 0.05

SBP systolic blood pressure, *IQR* interquartile range, *SD* standard deviation

Although there was no significant difference between age groups according to time of symptom evolution, radiological and laboratory findings related to a poor prognosis were more common with increasing age. This age association was clinically relevant in relation to lymphopenia ($P < 0.001$), thrombocytopenia ($P < 0.001$), a reduction in the glomerular filtration rate ($P < 0.001$), and an increase of lactate dehydrogenase ($P = 0.010$) and D-dimer values ($P < 0.001$) as well as C-reactive protein ($P < 0.001$) and procalcitonin ($P < 0.001$) (Table 3).

Concerning immediate treatment, there was greater use of hydroxychloroquine ($P < 0.001$), lopinavir/ritonavir ($P = 0.002$), corticosteroids ($P < 0.001$), azithromycin ($P < 0.001$), and other antibiotics ($P < 0.001$) with increasing age, with a sharp decline in the use of treatment for COVID-19 in the group ≥ 85 years of age (Table 3).

In-hospital and 30-day outcomes according to age-dependent categories

Among the 1379 patients, 1030 (74.6%) were hospitalized (5.9% in the ICU), and of these, 292 (21.9%) received high-flow oxygen or ventilation and 202 (14.6%) died during hospitalisation. During the 30-day follow-up, 217 (15.7%) patients died. A statistically significant linear trend was found between age-dependent groups and the likelihood of hospitalisation, and in-hospital and 30-day mortality (Table 3).

Table 3 Radiographic, laboratory, and treatment data and outcomes of the study population by age-dependent categories

	Patients N=1379 N (%)	18–44 years, N=250 n (%)	45–54 years, N=246 n (%)	55–64 years, N=247 n (%)	65–74 years, N=237 n (%)	75–84 years, N=235 n (%)	≥85 years, N=164 n (%)	P value
Chest X-ray								
No consolidation	407 (29.5)	100 (40.0)	78 (31.7)	70 (28.3)	57 (24.1)	62 (26.4)	40 (24.4)	**0.002**
Unilateral consolidation	311 (22.5)	57 (22.8)	55 (22.4)	48 (19.4)	60 (25.3)	44 (18.7)	46 (28.0)	
Bilateral consolidation	631 (45.7)	80 (32.0)	103 (41.9)	126 (51.0)	118 (49.8)	127 (54.0)	77 (47.0)	
Not done	31 (2.2)	13 (5.2)	10 (4.1)	3 (1.2)	2 (0.8)	2 (0.9)	1 (0.6)	
Laboratory data								
Leukocytes $\times 10^3$/ µL, [median (IQR)]	4.7 (6.1–8.3)	4.8 (6.0–7.8)	4.5 (6.1–7.6)	4.8 (6.4–8.7)	4.5 (5.4–8.1)	4.8 (6.3–8.5)	4.6 (6.4–9.1)	0.267
Hematocrit, % [median (IQR)]	42.0 (4.9)	43.4 (4.3)	43.3 (4.0)	42.8 (4.2)	41.6 (5.0)	40.9 (5.0)	39.5 (5.8)	**< 0.001**
Lymphocytes $\times 10^3$/ µL [median (IQR)]	0.6 (0.9–1.3)	0.8 (1.2–1.6)	0.8 (1.1–1.4)	0.7 (1.0–1.4)	0.6 (0.8–1.1)	0.5 (0.8–1.1)	0.5 (0.7–1.1)	**< 0.001**
Neutrophils $\times 10^3$/ µL [median (IQR)]	3.2 (4.4–6.6)	3.2 (4.2–5.6)	3.1 (4.3–5.8)	3.3 (4.5–7.0)	3.0 (4.1–6.6)	3.4 (4.7–6.6)	3.3 (4.7–7.4)	**0.003**
Platelet count $\times 10^3$/ µL [mean (SD)]	206.7 (88.6)	228.1 (77.8)	222.2 (97.2)	219.3 (93.4)	194.2 (85.9)	190.9 (87.8)	137 (224.5)	**< 0.001**
GFR (mL/ min/1,73 m2) [mean (SD)]	79.3 (27.9)	109.6 (15.1)	94.2 (20.2)	84.7 (22.2)	71.3 (23.5)	62.3 (23.7)	55.4 (21.7)	**< 0.001**
LDH, U/L [median (IQR)]	484 (624–825)	448 (565–708)	486 (607–806)	504 (647–844)	487 (638–867)	507 (656–874)	460 (621–842)	**0.010**
D-Dimer, ng/ ml [median (IQR)]	394 (657–1089)	293 (454–662)	340 (513–778)	360 (580–926)	476 (783–1380)	613 (912–1775)	652 (1140–1974)	**< 0.001**
C-reactive protein, mg/ dl [median (IQR)]	2.1 (5.9–12.3)	1.4 (4.0–8.9)	1.4 (3.5–9.5)	1.7 (6.5–11.6)	2.8 (6.3–14.8)	3.3 (8.1–14.1)	3.7 (8.1–13.7)	**< 0.001**
Procalcitonin, ng/ ml [median (IQR)]	0.0 (0.1–0.2)	0.0 (0.1–0.1)	0.0 (0.1–0.1)	0.0 (0.1–0.2)	0.0 (0.1–0.2)	0.1 (0.1–0.3)	0.1 (0.1–0.2)	**< 0.001**
Ferritin, ng/ ml [median (IQR)]	195 (490–958)	114 (378–736)	178 (461–849)	253 (532–1014)	335 (736–1118)	210 (487–1139)	202 (335–722)	**0.003**
AST, U/L [median (IQR)]	28 (38–55)	28 (36–55)	28 (38–58)	29 (39–60)	30 (40–60)	27 (38–53)	25 (34–45)	0.127

Table 3 (continued)

	Patients N = 1379 N (%)	18–44 years, N = 250 n (%)	45–54 years, N = 246 n (%)	55–64 years, N = 247 n (%)	65–74 years, N = 237 n (%)	75–84 years, N = 235 n (%)	≥85 years, N = 164 n (%)	P value
ALT, U/L [median (IQR)]	18 (28–46)	23 (34–60)	24 (35–58)	20 (30–52)	19 (29–46)	17 (24–36)	14 (17–27)	**< 0.001**
Bilirrubin, mg/dL [median (IQR)]	0.4 (0.5–0.7)	0.4 (0.4–0.6)	0.4 (0.6–0.7)	0.4 (0.5–0.7)	0.4 (0.6–0.7)	0.4 (0.6–0.8)	0.4 (0.6–0.7)	**< 0.001**
APTT ratio, [median (IQR)]	0.9 (1.0–1.1)	1.0 (1.0–1.1)	0.9 (1.0–1.1)	0.9 (1.0–1.1)	0.9 (1.0–1.1)	0.9 (1.0–1.1)	0.9 (1.0–1.1)	**0.006**
INR, [median (IQR)]	1.0 (1.1–1.2)	1.0 (1.1 -1.2)	1.0 (1.1 -1.2)	1.0 (1.1–1.2)	1.0 (1.1–1.2)	1.0 (1.1–1.3)	1.0 (1.1–1.5)	**< 0.001**
Fibrinogen, mg/dl [median (IQR)]	603 (714–836)	588 (718–810)	573 (705–833)	616 (748–892)	653 (746–846)	612 (713–823)	569 (656–727)	0.660
Treatment for COVID-19								
Hydroxychloroquine	979 (71.3)	129 (51.6)	162 (66.7)	186 (75.6)	201 (85.2)	195 (83.3)	105 (64.0)	**< 0.001**
Lopinavir/ ritonavir	627 (45.6)	105 (42.0)	119 (49.0)	135 (54.9)	130 (55.1)	98 (41.9)	39 (23.8)	**0.002**
Remdesivir	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.6)	0.152
Intravenous corticosteroid	273 (19.9)	16 (6.4)	27 (11.1)	67 (27.2)	69 (29.2)	64 (27.4)	30 (18.3)	**< 0.001**
Tocilizumab	74 (5.4)	3 (1.2)	16 (6.6)	32 (13.0)	15 (6.4)	8 (3.4)	0 (0.0)	0.269
Azithromycin	277 (20.2)	30 (12.0)	42 (17.3)	39 (15.9)	65 (27.5)	61 (26.1)	40 (24.4)	**< 0.001**
Another systemic antibiotic	598 (43.5)	52 (20.8)	70 (28.8)	97 (39.4)	133 (56.4)	145 (62.0)	100 (61.0)	**< 0.001**
Outcomes								
Hospital admission	1029 (74.6)	125 (50.0)	151 (61.4)	177 (71.7)	204 (86.1)	216 (91.9)	156 (95.1)	**< 0.001**
Critical care admission	82 (5.9)	8 (3.2)	15 (6.1)	30 (12.1)	21 (8.9)	8 (3.4)	0 (0.0)	0.151
Need to high-flow oxygen or ventilation	292 (22.0)	10 (4.1)	25 (10.5)	56 (23.7)	64 (28.1)	86 (37.9)	51 (32.5)	**< 0.001**
In-hospital mortality	202 (14.6)	0 (0.0)	4 (1.6)	10 (4.0)	38 (16.0)	76 (32.3)	74 (45.1)	**< 0.001**
30-day mortality	217 (15.7)	1 (0.4)	6 (2.4)	13 (5.3)	40 (16.9)	79 (33.6)	78 (47.6)	**< 0.001**

P value for lineal trend. Numbers in bold mean value *P* < 0.05

GFR glomerular filtration rate, *LDH* lactate dehydrogenase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *SD* standard deviation, *IQR* interquartile range

Kaplan–Meier survival curves showed statistically significant differences between each age group and the 30-day mortality outcome (P < 0.001) (Fig. 2). The oldest age groups were associated with the poorest outcomes.

The forest plot reflects the univariable and multivariable associations between each age, as a continuous variable, and the primary and secondary outcomes. After adjustment for potential confounding factors, age remained significantly associated with hospital admission and in-hospital and

30-day mortality and was associated with not being admitted to intensive care (Fig. 3).

Discussion

The main finding of this study is that age determines the profile, management, and short-term health outcomes among COVID-19 patients admitted to the ED. This study provides information on the process of care for older patients with COVID-19 in the ED, which can be useful to develop accurate diagnosis and treatment strategies when designing future protocols.

Comorbidities such as hypertension, obesity, diabetes, chronic cardiovascular and respiratory disease, cerebrovascular disease, dementia, kidney disease, immunosuppressive conditions, and cancer have been described as prognostic factors in COVID-19 [9] irrespectively of age [14]. Although these conditions were more frequent as age increased, age was also associated with poor in-hospital and 30-day outcomes after adjustment for sex, comorbidities, and severity, thereby strengthening the evidence that age is an independent prognostic factor in COVID-19 [9, 15]. However, other circumstances related to ageing such as the degree of frailty or malnutrition also likely facilitate a worse course of the disease. Immunosenescence may produce a state of vulnerability to infectious disease due to slow, incoordinate, and inefficient immune response to SARS-Cov-2 [8]. In addition, the physiological changes induced by ageing may favour delay in diagnosis and misdiagnosis [4, 7, 14, 16]. In fact, at arrival to the ED, the oldest groups more frequently had an atypical presentation, hypoxemia [17] and other abnormal radiological [18] and laboratory [15] findings associated with severe COVID-19.
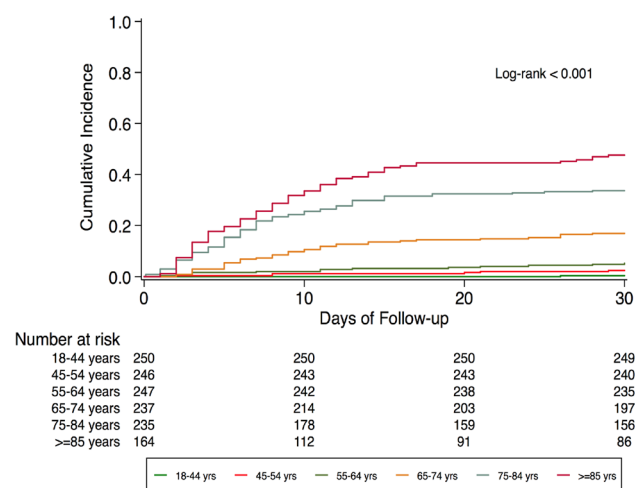
Fig. 2 Cumulative 30-day mortality curves for each age group
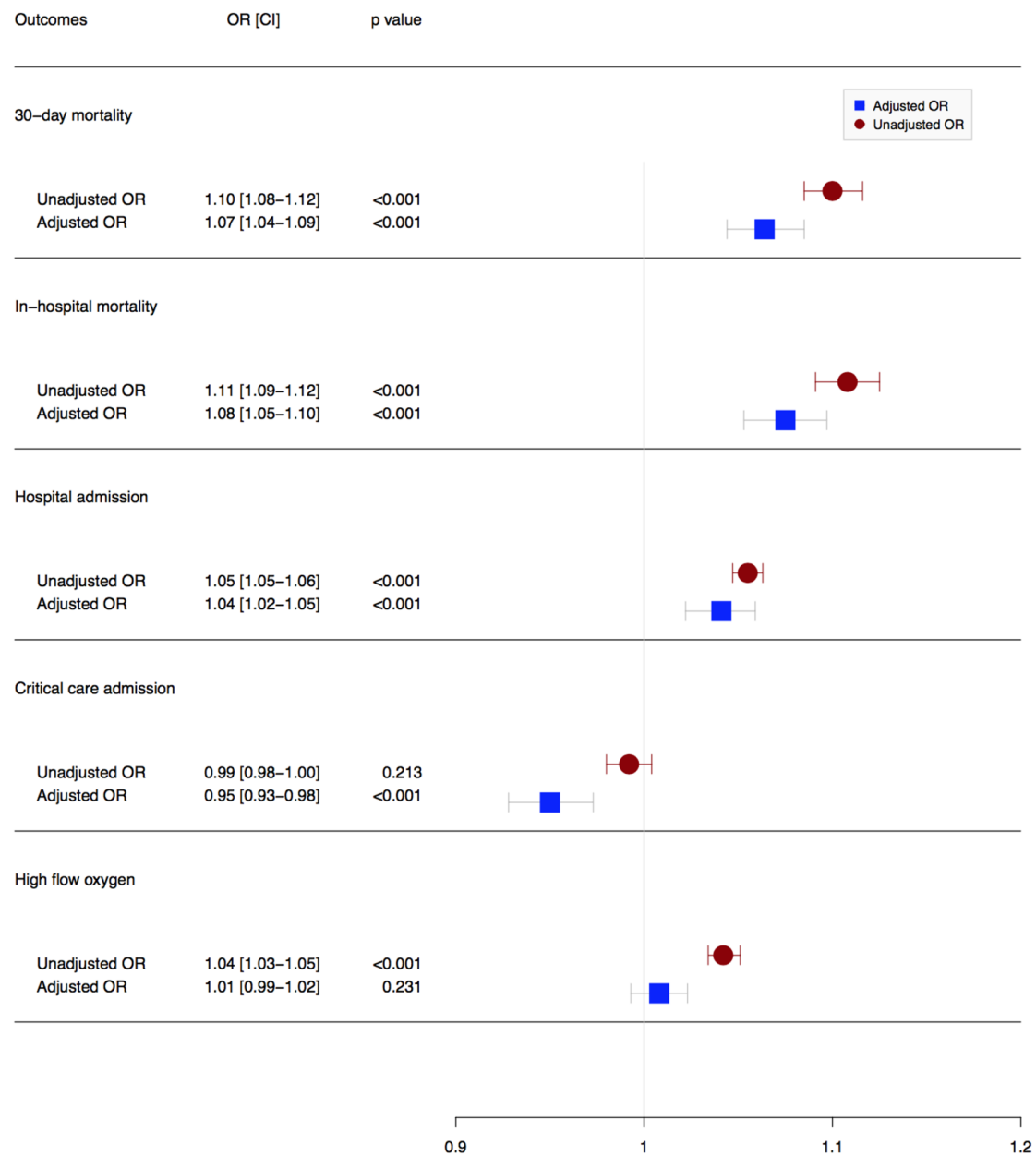
The clinical presentation on ED arrival differed between age groups. Subjective fever (80%), cough (71%), and dyspnoea (47%) were the most common symptoms of presentation in our population similar to what has been described in the previous studies [5, 16, 19–21]. However, the presence of these core symptoms of COVID-19 was less common with increasing age. In addition, the older groups more frequently had unspecific findings such as asthenia or atypical presentations such as confusion and presyncope or syncope. This confirms the previous case reports which have described the importance of delirium and syncope (near-syncope and falls) as the first presentations in older patients with COVID-19 [22–24].

Regarding vital signs at arrival to the ED, the mean oxygen saturation and body temperature showed an inverse correlation with age. Although there was no relation between dyspnoea and age groups, hypoxemia was more common with increasing age. It is essential to take this circumstance into account, since a lack of subjective shortness of breath may delay the diagnosis of COVID-19, and hypoxemia is a recognized prognostic factor in COVID-19 [17]. With respect to body temperature, the previous studies have shown that older people are less likely to develop fever with an infectious disease [25]. This has also been reported in COVID-19 [17]. The lack of this cardinal sign may increase the difficulty in diagnosing COVID-19. Indeed, some authors have suggested that the usual temperature threshold for fever in older patients be modified [26].

Although no differences were found between the mean time from symptom onset to arrival at the ED, radiological findings and laboratory determinations related to the severity of COVID-19 were more common with increasing age. The previous studies have reported that older patients were more likely to suffer severe pneumonia [27–29], lymphopenia, and elevation of inflammatory markers in comparison with younger patients [4]. This state may be related to a worse host response against infection or a further diagnostic delay in older patients with COVID-19.

Considering that the diagnosis of COVID-19 is more complicated in older patients, emergency physicians need to use a combination of high clinical suspicion, radiological and laboratory tests, and RT-PCR results to allow early diagnosis, isolation, infection control measures, and provision of supportive care. Some clinical and laboratory abnormalities more frequent in older patients who died, and this should be considered in older aged patients due to the consequent worse prognosis. In our population, the frequency of the use of RT-PCR increased with age, as did the non-conclusive results. In this sense, a negative nasopharyngeal swab should not exclude COVID-19 infection if there is high clinical suspicion or an atypical presentation [30, 31].

Although there is no specific treatment for COVID-19, the use of hydroxychloroquine, antivirals, corticosteroids,

Outcomes	OR [CI]	p value
30–day mortality		
Unadjusted OR	1.10 [1.08–1.12]	<0.001
Adjusted OR	1.07 [1.04–1.09]	<0.001
In–hospital mortality		
Unadjusted OR	1.11 [1.09–1.12]	<0.001
Adjusted OR	1.08 [1.05–1.10]	<0.001
Hospital admission		
Unadjusted OR	1.05 [1.05–1.06]	<0.001
Adjusted OR	1.04 [1.02–1.05]	<0.001
Critical care admission		
Unadjusted OR	0.99 [0.98–1.00]	0.213
Adjusted OR	0.95 [0.93–0.98]	<0.001
High flow oxygen		
Unadjusted OR	1.04 [1.03–1.05]	<0.001
Adjusted OR	1.01 [0.99–1.02]	0.231

*Adjusted by sex, hypertension, diabetes, dyslipemia, obesity, chronic respiratory disease, heart disease, cerebrovascular disease, dementia, chronic renal disease, dependency on basic activities of daily living, oxygen saturation on arrival, abnormal chest x-ray, lymphocytes, platelet count, glomerular filtration rate, lactate dehydrogenase, D-Dimer, C-reactive protein and procalcitonin.

Fig. 3 Estimated unadjusted and adjusted Odds ratios for the association between age, as continues variables, and different outcomes

and antibiotics increased with age until 85 years old. After this age, the prescription of azithromycin and other antibiotics continued to increase but not the administration of hydroxychloroquine, lopinavir/ritonavir, or corticosteroids. This reduction may be related to the presence of more comorbidities and polypharmacy in these patients, which could favour drug interactions [32] as well as cautious use of corticosteroids to decrease the risk of adverse events or viral replication [33]. Regarding medication management in older adults during COVID-19, pharmacokinetics and drug interactions and medication reviews must be considered because of the increased risk of drug-related adverse events in older patients [33].

Patients should receive supportive care to help relieve symptoms, including care to support vital organ functions. In our study, age was a factor associated with not

being admitted to intensive care, similar to what has been described in other series [4]. In this respect, it is striking that physicians have frequently faced complex decisions to determine who could most benefit from intensive care and ventilatory support in an overrun situation of health services and ICUs [34, 35]. Prioritisation for ventilators or intensive care should not be based on chronological age. This age cut-off ignores the enormous heterogeneity of functional status, cognitive status, and burden of comorbidities in older populations [36]. Experts recommend a more holistic evaluation based on degree of frailty, the likelihood of medical interventions being successful, and the severity of the presenting acute illness to ensure the optimisation of available resources [37–39]. Decisions must be made on the basis of futility versus those based on rationing [40].

Our study has several limitations. First, this was a retrospective observational study and causal relationships between age and outcomes cannot be inferred. Second, the order of the diagnostic tests was determined by public health recommendations. In addition, the performance of RT-PCR in our centre may differ from the use of other diagnostic tests. These circumstances may have modified the categorisation of the patients and, therefore, this may have selected the population included in the study. Third, our study included information about patients who presented at the ED of one public hospital located in the centre of Madrid. This may introduce some degree of selection bias, since COVID-19 patients with mild symptoms could have been attended by EMS or GPs. The findings may be representative of what has happened in an urban and tertiary ED providing health care to one of the nuclei of the pandemic in Madrid. Fourth, this study was performed in an overcrowded ED during the COVID-19 pandemic. This may introduce some degree of information bias because of the high number of people involved in data collection. However, all the investigators involved in the collection of data had received the previous training and all the information was checked by a trained researcher. Fifth, this is a real-life cohort in which attending physicians followed the interventions of the local protocol. In addition, the recommendations on treatment for COVID-19 varied during the study period. Although this imposes limitations to our study, there is currently no evidence related to a specific drug, thereby making our findings more generalisable.

In conclusion, clinical presentation, management, and short-term outcomes of patients with COVID-19 admitted to the ED differs according to age-dependent categories. Age has an independent prognostic value and may help in shared decision-making. Further studies in older people with COVID-19 are needed to determine the factors associated with these poor outcomes.

Compliance with ethical standards

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