

# Baseline characteristics and outcome predictors in patients hospitalized with COVID-19 in the University General Hospital of Ioannina, Greece

Vitaliano N. Quaranta<sup>1,2</sup>, Christos Kyriakopoulos<sup>1</sup>, Angelos Lontos<sup>3</sup>, Fotios Barkas<sup>3</sup>, Christos Chronis<sup>1</sup>, Dimitrios Biros<sup>3</sup>, Lazaros Athanasiou<sup>3</sup>, Orestis Milionis<sup>3</sup>, Stavros Tsourlos<sup>3</sup>, Cornelia Veliani<sup>3</sup>, Alexandros Papatheanasiou<sup>3</sup>, Valentini Samanidou<sup>3</sup>, Agapi Aggelopoulou<sup>1</sup>, Vanesa Bellou<sup>1</sup>, Nikolaos-Gavriil Kolios<sup>3</sup>, Christiana Pappa<sup>3</sup>, Sempastien Filippas-Ntekouan<sup>3</sup>, Giovanna E. Carpagnano<sup>2</sup>, Silvano Dragonieri<sup>2</sup>, Eirini Christaki<sup>3</sup>, Athanasios Konstantinidis<sup>1</sup>, Haralampos Milionis<sup>3</sup>, Konstantinos Kostikas<sup>1</sup>

## ABSTRACT

**INTRODUCTION** The novel Severe Acute Respiratory Syndrome Coronavirus-2, which causes the coronavirus disease COVID-19, is a highly infectious viral pathogen that is responsible for the ongoing pandemic. The aim of the present study was to illustrate the pre-hospitalization baseline characteristics and comorbidities of patients admitted with COVID-19 and their association with patient outcomes.

**METHODS** This was a retrospective observational study of consecutive patients who were admitted to the COVID-19 departments of the University General Hospital of Ioannina, Greece (March 2020 – August 2021). Patients' demographic data, chronic disease medication use, and comorbidities were recorded upon their admission.

**RESULTS** A total of 627 patients were hospitalized with mean age 62.5 years, 65.2% with at least one comorbidity, and 43.1% female. The median hospitalization duration was 11 days; 554 (88.4%) of the patients were discharged and the mortality rate was 11.6%. Older age, admission during the second pandemic wave, arterial hypertension, and diabetes mellitus were associated with longer hospitalization. In multivariate analyses, cardiovascular disease was an independent predictor of hospitalization length (OR=1.834; 95% CI: 1.039–3.228), whereas age (HR=1.079; 95% CI: 1.045–1.115), history of malignancy (HR=1.246; 95% CI: 1.002–1.595), and a diagnosis of COPD (HR=1.989; 95% CI: 1.025–7.999) remained the independent mortality predictors.

**CONCLUSIONS** Our data highlight the effect of COPD and malignancy on mortality risk in COVID-19 patients and the association of cardiovascular disease with a longer hospitalization.

## INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which is the causing agent of coronavirus disease COVID-19, is an extremely infectious viral pathogen accounting for the current pandemic<sup>1</sup>. Up to 1 November 2021, more than 251 million infections with SARS-CoV-2 were reported globally, with 5 million deaths worldwide attributable to COVID-19<sup>2</sup>. The clinical manifestations of COVID-19 demonstrate high diversity, ranging from asymptomatic infection to acute respiratory distress syndrome (ARDS), and death. Despite being usually asymptomatic, COVID-19 can also present with mild symptoms, taste and smell changes, myalgias, or moderate pneumonia. Occasionally, COVID-19 appears as severe pneumonia and ARDS, primarily affecting individuals

with comorbidities and older patients, leading to high mortality<sup>3</sup>. Cardiovascular disease, chronic respiratory diseases, obesity, diabetes mellitus, chronic kidney disease, severe immunosuppression, hematologic or solid organ malignancy have been associated with disease severity<sup>4-6</sup>. Moreover, disease progression and worse hospitalization outcomes have been attributed to male sex, advanced age, obesity, being non-White, smoking history, Alzheimer's disease, Parkinson's disease, COPD, diabetes, hypertension, malignancy, coronary heart disease, and chronic kidney disease<sup>7-9</sup>. Currently there is no specific treatment for COVID-19 available and should be principally managed by vaccination, preventing the transmission of the virus by averting the exposure, and smoking cessation<sup>10</sup>. Previous studies have demonstrated a survival benefit by

## AFFILIATION

**1** Department of Respiratory Medicine, Faculty of Medicine, University of Ioannina, Ioannina, Greece

**2** Department of Respiratory Diseases, University of Bari, Bari, Italy

**3** 1st Internal Medicine Department, Faculty of Medicine, University of Ioannina, Ioannina, Greece

## CORRESPONDENCE TO

Christos Kyriakopoulos. Department of Respiratory Medicine, Faculty of Medicine, University of Ioannina, Stavrou Niarchou Avenue, 45500, Ioannina, Greece.  
E-mail: ckyriako@yahoo.gr  
ORCID ID: <https://orcid.org/0000-0001-8806-2561>

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administering dexamethasone and tocilizumab in patients that require oxygen therapy or invasive mechanical ventilation (IMV), while the duration of hospitalization can be reduced by remdesivir<sup>11-13</sup>. COVID-19 patients often develop secondary bacterial infections in the course of their hospitalization, especially during ICU stay<sup>14</sup>.

Up to 1 November 2021, there were more than 745000 SARS-CoV-2 documented infections in Greece resulting in more than 16000 deaths. During the same period in the region of Epirus, northwestern Greece, where the University General Hospital of Ioannina serves as a referral center for patients with COVID-19, 14050 cases and 302 deaths have been confirmed<sup>15,16</sup>. In the present study, we illustrate the pre-hospitalization baseline characteristics and comorbidities of patients admitted with COVID-19 to the University Hospital of Ioannina during the first 4 waves of the pandemic, and to analyze how these might have influenced the clinical outcomes of these patients.

## METHODS

In the present retrospective observational study of all consecutive patients admitted to the COVID-19 infectious diseases units of the University General Hospital of Ioannina (March 2020 – August 2021), subjects' demographic data were recorded upon their admission including sex, age, body mass index (BMI, kg/m<sup>2</sup>), treatment prior to admission, comorbidities, and smoking status. Upon admission we recorded additionally clinical parameters; more specifically vital signs, the presence of dyspnea, and the level of respiratory failure.

The following pre-hospitalization parameters were recorded: demographics; date of admission defining in which COVID wave the admission took place; lifestyle risk factors; BMI with obesity being defined as BMI  $\geq 30$  kg/m<sup>2</sup>; cigarette smoking habit; history of comorbidities (i.e. hypertension, COPD, asthma, diabetes, malignancy, atherosclerotic cardiovascular disease); type of drug therapy chronically taken at home (the chronically received medication for past medical history). COVID-19 waves were defined as follows: 1st wave March 2020 – August 2020; 2nd wave September 2020 – December 2020; 3rd wave January 2021 – April 2021; and 4th wave May 2021 – August 2021.

We classified patients in three groups based on their outcomes (discharge, death, and intubation and admission to ICU with subsequent discharge) and compared them with each other. The predictors of these outcomes, along with the length of hospitalization were investigated.

## Statistical analysis

We used the Shapiro-Wilk and Kolmogorov-Smirnov tests to evaluate if the data had a normal distribution. The chi-squared or Fisher's exact tests, as appropriate, were used to analyze categorical values, reported as n (%), while continuous variables were analyzed by Student's t-test (for independent samples of normally distributed data) or by

Mann-Whitney U and Kruskal-Wallis tests (for independent samples of non-normally distributed data). We performed univariate and multivariate binomial logistic regression analyses in order to define the parameters predicting mortality starting from the pre-admission parameters considered in the study (demographics, comorbidities, risk factors, chronic disease medication use). Patients were divided in two groups based on the median duration of hospitalization (11 days) to perform the multivariate analysis of length of hospitalization. All statistical analyses were performed using SPSS for Windows 23.0 (SPSS, Chicago, Illinois), with the level of statistical significance set at  $p < 0.05$ .

## RESULTS

### Demographics and baseline characteristics

The mean (SD) age of the 627 study participants was 62.5 (16.6) years (76.5% were aged >50 years) and 270 (43.1%) were female. Nineteen patients (3%) were hospitalized during the 1st COVID wave, 206 (32.9%) during the 2nd wave, 295 (47%) during the 3rd wave and 107 (17.1%) during the 4th wave (Tables 1 and 2). The mean (SD) duration of symptoms before hospitalization was 6.66 (0.20) days, with fever being the most frequent symptom (82.7% of the cases) (Table 1). Upon admission the majority of the patients presented with moderate (32.9%) and severe (42.8%) COVID-19 disease (Table 2).

### Comorbidities

A total of 409 (65.2%) subjects had at least one comorbidity. Comorbidities most commonly present were arterial hypertension (AH), dyslipidemia, obesity, and diabetes mellitus (DM) (Table 1). Drugs most frequently prescribed were statins and angiotensin II receptor antagonists/ACE inhibitors (Table 1).

### Hospitalization outcome

The mean (SD) duration of hospitalization was 13.13 (8.54) days, with a median of 11 days (IQR: 7.00–17.25). All 627 patients were initially admitted to the COVID-19 infectious diseases units, while 48 (7.7%) were transferred to the ICU section during their hospitalization. Finally, 537 (85.7%) were discharged, 17 (2.7%) were intubated or admitted to the ICU and subsequently discharged, and 73 (11.6%) did not survive (Figure 1, Table 2). Among those who died, 43 (6.9%) patients died in the infectious disease units and 31 (4.9%) in the ICU. The intubation rates were 0%, 3.9%, 2.3%, and 1.8% during the 1st, 2nd, 3rd, and 4th pandemic waves in Greece. The mortality rates were 11.1%, 17.5%, 10.2% and 4.7%, respectively (Figure 2, Table 2).

### Comparison between groups

*Comparison between discharged, deceased, and intubated/ICU patients*

In the comparative analysis, a higher proportion of patients

**Table 1. Baseline characteristics of the study participants (N=627)**

Characteristics	n (%)
<b>Demographics</b>	
Age (years), mean ± SD	62.65 ± 16.63
Female	270 (43.1)
Smokers	81 (12.9)
BMI, mean ± SD	29.45 ± 5.42
<b>Comorbidities</b>	
Obesity	194 (31.0)
Age (years) >50	480 (76.5)
Diabetes	132 (21.1)
CVD	120 (19.1)
Arterial hypertension	279 (44.5)
Dyslipidemia	215 (34.3)
COPD	32 (5.1)
CKD	30 (4.8)
Autoimmune disease	26 (4.2)
Immunosuppression	37 (5.9)
Cancer	30 (4.8)
Thyroid disease	67 (10.7)
<b>Medication</b>	
Statins	199 (31.8)
ACE inhibitors	54 (8.7)
Angiotensin II receptor antagonists	183 (29.3)
B-blockers	120 (19.2)
Corticosteroids	38 (6.1)
Symptoms duration before hospitalization (days), mean ± SD	6.66 ± 0.20
<b>Symptoms</b>	
Fever	519 (82.7)
Dry cough	313 (49.9)
Fatigue	170 (27.1)
Anorexia	48 (7.6)
Myalgias	100 (15.9)
Dyspnea	167 (26.6)
Sputum production	46 (7.3)
Anosmia	51 (8.13)
Dysgeusia	58 (9.2)
Gastrointestinal symptoms	205 (32.7)
Headache	51 (8.1)
Sore throat	37 (5.9)
Rhinorrhea	12 (1.9)

CVD: cardiovascular disease. AH: arterial hypertension. COPD: chronic obstructive pulmonary disease. CKD: chronic kidney disease. BMI: body mass index (kg/m<sup>2</sup>).

who died was diagnosed with some comorbidity (Table 3). More specifically, the deceased patients had a higher probability to be older and present with at least one comorbidity compared with the other two groups. Likewise, a higher proportion of these were diagnosed with AH, DM COPD, cancer, CKD, immunosuppression and treated with corticosteroids (Table 3).

#### *Comparison within discharged patients based on length of hospitalization*

Among the 537 discharged patients the median duration of hospitalization was 11 days (IQR: 7–16). Older age and admission during the second wave were associated with a longer hospitalization ( $\geq 11$  days) (Table 4). Furthermore, patients with a longer hospital stay ( $\geq 11$  days) were more likely to have at least one comorbidity compared with those hospitalized <11 days (68.5 vs 49.1%,  $p < 0.001$ ). Similarly, arterial hypertension and diabetes mellitus were associated with longer hospitalization (Table 4).

#### **Predictors of hospitalization outcomes**

##### *Predictors of longer hospitalization*

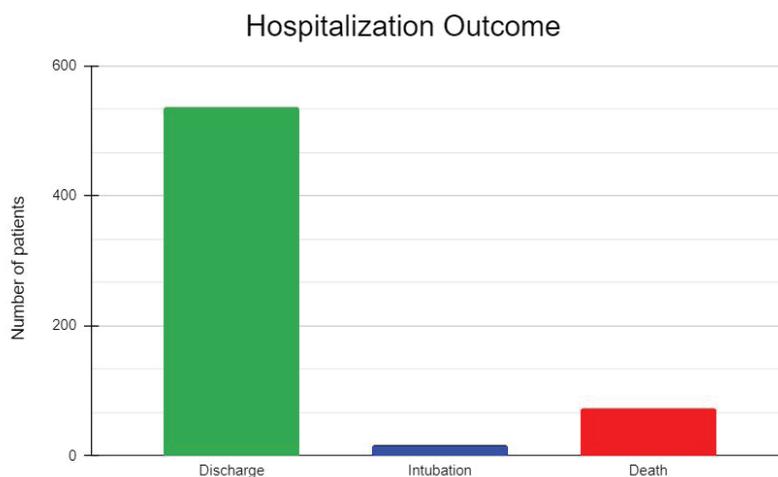
In the univariate regression analyses, duration of hospitalization was associated with age, arterial hypertension, diabetes, and the presence of at least one comorbidity. In the multivariate logistic regression analyses, only cardiovascular disease remained as an independent predictor of longer hospitalization (OR=1.834; 95% CI: 1.039–3.228) (Table 5).

**Table 2. Admissions per COVID-19 wave and hospitalization outcome (N=627)**

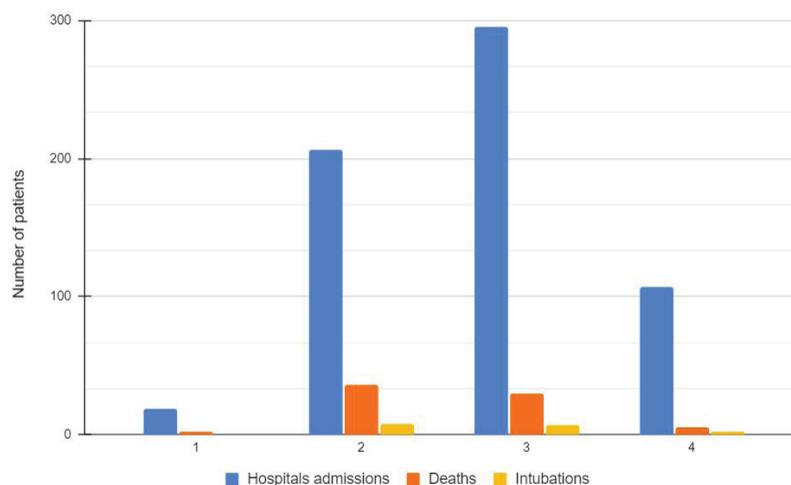
Variables	n (%)
<b>Admissions COVID-19 wave</b>	
1st	19 (3.0)
2nd	206 (32.9)
3rd	295 (47.0)
4th	107 (17.1)
<b>COVID-19 severity upon admission</b>	
Asymptomatic	15 (2.3)
Mild	78 (12.5)
Moderate	206 (32.9)
Severe	269 (42.8)
Critical	59 (9.5)
<b>Hospitalization outcome</b>	
Hospitalization duration (days), mean ± SD	13.13 ± 8.54
Discharge	537 (85.7)
Intubation/ICU	17 (2.7)
Death	73 (11.6)*

\*Of these, 31 patients were previously intubated.

**Figure 1. Hospitalization outcome for patients with COVID-19 who were admitted in the infectious disease units of the University Hospital of Ioannina from March 2020 to August 2021**



**Figure 2. Admissions, number of deaths and intubations per COVID-19 wave in the University Hospital of Ioannina**



**Table 3. Comparison between deceased, intubated/ICU, discharged patients (N=627)**

Parameters	Death (n=73) n (%)	Intubation/ICU (n=17) n (%)	Discharged (n=537) n (%)	p
<b>Age</b> (years) <sup>ab</sup> , mean ± SD	77.58 ± 11.51	63.29 ± 8.1	60.60 ± 16.39	<b>&lt;0.001</b>
Female	40 (54.8)	6 (35.3)	224 (41.7)	0.086
<b>COVID-19 wave<sup>b</sup></b>				<b>0.020</b>
1st	2 (2.9)	0 (0)	17 (3.1)	
2nd	36 (49.3)	8 (47.1)	162 (30.3)	
3rd	30 (42.0)	7 (41.1)	258 (48.0)	
4th	5 (5.8)	2 (11.8)	100 (18.6)	
<b>Obesity</b>				0.097
Yes	14 (19.2)	7 (41.2)	173 (32.1)	
No	59 (80.8)	10 (58.8)	364 (67.9)	

Continued

Table 3. Continued

Parameters	Death (n=73) n (%)	Intubation/ICU (n=17) n (%)	Discharged (n=537) n (%)	p
BMI, mean ± SD	27.35 ± 6.11	29.52 ± 5.49	29.58 ± 5.37	0.249
<b>Age (years) &gt;50<sup>b</sup></b>				<b>&lt;0.001</b>
Yes	72 (98.6)	16 (94.1)	392 (73.0)	
No	1 (1.4)	1 (5.9)	145 (27.0)	
<b>Comorbidities ≥1<sup>b</sup></b>				<b>&lt;0.001</b>
Yes	64 (87.7)	13 (76.5)	332 (58.0)	
No	9 (12.3)	4 (23.5)	241 (42.0)	
<b>DM<sup>b</sup></b>				<b>0.048</b>
Yes	23 (31.5)	2 (11.8)	108 (20.1)	
No	50 (68.5)	15 (88.2)	429 (79.1)	
<b>Cancer<sup>b</sup></b>				<b>0.002</b>
Yes	9 (12.3)	2 (11.8)	19 (3.5)	
No	64 (87.7)	15 (88.2)	518 (96.5)	
<b>Autoimmune disease</b>				0.530
Yes	2 (2.7)	0 (0)	24 (4.5)	
No	71 (97.3)	17 (100)	513 (95.5)	
<b>Cardiovascular disease<sup>b</sup></b>				<b>&lt;0.001</b>
Yes	29 (39.7)	4 (23.5)	87 (16.2)	
No	44 (60.3)	13 (76.5)	450 (83.8)	
<b>Thyroid disease</b>				0.627
Yes	14 (19.2)	7 (41.1)	67 (12.5)	
No	59 (80.8)	10 (58.9)	470 (87.5)	
<b>Arterial hypertension<sup>b</sup></b>				<b>0.002</b>
Yes	42 (57.5)	10 (58.9)	227 (42.3)	
No	31 (42.5)	7 (41.1)	310 (57.7)	
<b>COPD<sup>b</sup></b>				<b>0.001</b>
Yes	10 (13.7)	0 (0)	22 (4.1)	
No	63 (86.3)	17 (100)	515 (95.9)	
<b>Dyslipidemia</b>				0.428
Yes	30 (41.1)	6 (35.3)	179 (33.3)	
No	43 (58.9)	11 (64.7)	358 (66.7)	
<b>Smoking</b>				0.664
Yes	8 (11.0)	1 (5.9)	72 (13.5)	
No	65 (89.0)	16 (94.1)	465 (86.5)	
<b>Chronic kidney disease<sup>b</sup></b>				<b>0.004</b>
Yes	9 (12.3)	0 (0)	21 (3.9)	
No	64 (87.7)	17 (100)	516 (96.1)	
<b>Immunosuppression<sup>b</sup></b>				<b>0.042</b>
Yes	9 (12.3)	1 (5.9)	27 (5.0)	
No	64 (87.7)	16 (94.1)	510 (95.0)	
<b>Corticosteroids<sup>b</sup></b>				<b>0.001</b>
Yes	11 (15.1)	2 (11.8)	25 (4.7)	
No	62 (84.9)	15 (88.2)	512 (95.3)	

COPD: chronic obstructive pulmonary disease. BMI: body mass index (kg/m<sup>2</sup>). a Comparison between deceased group and ICU/intubation group: significant difference with p<0.050.

b Comparison between deceased group and discharged group: significant difference with p<0.050.

**Table 4. Comparison within discharged patients based on length of hospitalization**

Variables	Hospitalization days <11 (n=262) %	Hospitalization days ≥11 (n=275) %	p
<b>Male</b>	56.7	59.6	0.295
<b>Age</b> (years), mean ±SD	55.88 ± 16.32	66.23 ± 14.20	<b>&lt;0.001</b>
<b>Age</b> (years) >50	62.7	85.5	<b>&lt;0.001</b>
<b>COVID-19 wave</b>			
1st	4.4	3.3	<b>0.001</b>
2nd	29.1	41.6	
3rd	51.5	50.5	
4th	15.0	4.7	
<b>Smokers</b>	14.8	14.5	0.513
<b>Presence of comorbidities</b>	49.1	68.5	<b>&lt;0.001</b>
<b>Autoimmune disease</b>	6.9	3.6	0.086
<b>BMI</b> , mean ± SD	29.01 ± 4.83	29.84 ± 5.37	0.248
<b>Comorbidities</b>			
Obesity	31.1	31.7	0.491
CVD	11.6	24.2	<b>&lt;0.001</b>
Cancer	2.3	5.8	0.052
DM	15.3	22.8	<b>0.029</b>
AH	34.1	47.8	<b>0.002</b>
COPD	3.2	5.7	0.151
Dyslipidemia	31.5	36.4	0.160
CKD	2.8	6.1	0.067
Immunosuppression	5.1	6.2	0.384
Oral corticosteroids	3.7	7.0	0.089

CVD: cardiovascular disease. AH: arterial hypertension. COPD: chronic obstructive pulmonary disease. CKD: chronic kidney disease. BMI: body mass index (kg/m<sup>2</sup>).

**Table 5. Predictors of longer hospitalization**

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Male	0.885 (0.607–1.290)	0.885	NE	
Age (years)	1.972 (0.826–4.706)	<b>&lt;0.001</b>	1.594 (0.886–2.869)	0.120
Smoking	0.973 (0.575–1.647)	0.919	NE	
Presence of comorbidities	2.222 (1.507–3.275)	<b>&lt;0.001</b>	1.152 (0.602–2.202)	0.670
Autoimmune disease	0.890 (0.769–1.031)	0.121	NE	
Obesity	1.027 (0.685–1.539)	0.699	NE	
CVD	2.441 (1.455–4.095)	<b>0.001</b>	1.834 (1.039–3.228)	<b>0.037</b>
Cancer	1.212 (0.992–1.495)	0.073	NE	
DM	1.638 (1.011–2.655)	<b>0.045</b>	1.104 (0.646–1.885)	0.450
AH	1.770 (1.207–2.595)	<b>0.033</b>	0.704 (0.507–1.608)	0.450
COPD	1.814 (0.710–4.636)	0.214	NE	
Dyslipidemia	1.246 (0.840–1.847)	0.274	NE	
CKD	2.301 (0.868–6.100)	0.094	NE	
Immunosuppression	1.231 (0.546–2.774)	0.616	NE	
Oral corticosteroids	1.972 (0.826–4.706)	0.126	NE	

CVD: cardiovascular disease. AH: arterial hypertension. COPD: chronic obstructive pulmonary disease. CKD: chronic kidney disease. NE: not entered in the multivariate analysis.

Table 6. Predictors of mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Male	1.708 (1.045–2.790)	<b>0.033</b>	1.430 (0.719–2.847)	0.308
Age (years)	1.086 (1.063–1.109)	<b>&lt;0.001</b>	1.086 (1.053–1.121)	<b>&lt;0.001</b>
Length of hospitalization	1.037 (1.008–1.067)	<b>0.001</b>	0.992 (0.952–1.033)	0.669
Presence of comorbidities	5.029 (2.452–10.312)	<b>&lt;0.001</b>	1.012 (0.976–1.049)	0.522
CVD	3.310 (1.968–5.667)	<b>&lt;0.001</b>	1.846 (0.829–4.114)	0.134
Cancer	1.287 (1.092–1.517)	<b>0.003</b>	1.246 (1.002–1.595)	<b>0.048</b>
Obesity	0.540 (0.292–1.000)	<b>0.050</b>	0.410 (0.159–1.059)	0.066
Age (years) ≥50	25.765 (3.548–187.085)	<b>0.001</b>	1.743 (0.824–3.686)	0.146
DM	1.874 (1.096–3.204)	<b>0.022</b>	0.667 (0.300–1.482)	0.320
AH	1.812 (1.106–2.969)	<b>0.018</b>	1.988 (0.653–6.057)	0.226
COPD	3.838 (1.739–8.473)	<b>0.001</b>	1.989 (1.025–7.999)	<b>0.045</b>
CKD	3.569 (1.568–8.127)	<b>0.002</b>	1.928 (0.530–7.588)	0.305
Oral corticosteroids	3.450 (1.631–7.295)	<b>0.001</b>	1.666 (0.486–5.711)	0.417

CVD: cardiovascular disease. AH: arterial hypertension. COPD: chronic obstructive pulmonary disease. CKD: chronic kidney disease. HR: mortality risk.

### Predictors of mortality

In the univariate regression analyses, male sex, advanced age, length of hospitalization, CVD, cancer, DM, arterial hypertension, COPD, CKD, the absence of obesity, and oral corticosteroids prior to admission were associated with mortality risk (Table 6). In multivariate binomial logistic regression analyses, age (HR=1.079; 95% CI: 1.045–1.115), history of malignancy (HR=1.246; 95% CI: 1.002–1.595), and COPD (HR=1.989; 95% CI: 1.025–7.999) remained as independent predictors of mortality (Table 6).

## DISCUSSION

In the present retrospective analysis of prospectively collected data of 627 patients who were hospitalized with COVID-19 at the University Hospital of Ioannina during the period March 2020 – August 2021, the mortality rate was 11.6%. The majority of the patients in our population presented with severe COVID-19 pneumonia and respiratory failure upon admission (42.8%), while 168 (26.8%) of the patients progressed to critical disease during hospitalization. Older age, COPD and a history of malignancy were independent predictors of mortality. The median duration of hospitalization in our study was 11 days and the presence of cardiovascular disease was associated with a longer hospitalization.

Mortality among critically ill patients with COVID-19 varies significantly between published case series and ranges from 16% to 78%<sup>17-20</sup>. In an Italian case series of 96 patients admitted to Respiratory Intermediate Care Unit (RICU), the mortality was 46%, which increased further in ICU patients<sup>21</sup>. Our lower mortality rate (11.6% overall and 6.9% outside

the ICU) could be attributed to the fact that our study did not refer exclusively to patients hospitalized in respiratory ICUs. This is despite the fact that many of our patients with severe or critical respiratory failure were managed in our non-ICU COVID-19 wards. These relatively good results may, at least partially, be attributed to the multidisciplinary patient management which led to the early implementation of specialist knowledge by the medical teams exchanging experiences and sharing treatment decision-making in three weekly multidisciplinary meetings. They could also be associated with the different COVID-19 variants and the different periods of the year that each study was held.

In our population with a mean age of 63 years, COPD was a comorbidity in 5.1%, in accordance with published results. For instance, in New York City the prevalence of COPD among hospitalized patients ranged from 2.4% to 14%, in Italy from 5.6 to 9.2%, and in China up to 10%<sup>22</sup>. In southern Italy, during the first COVID wave, the prevalence of respiratory diseases was 8.3%<sup>23</sup>. Among COPD patients it is known from the literature that severe physiological imbalance upon admission to ICU, severity of COPD disease and high comorbid burden are predictors of mortality in critically ill patients with acute COPD exacerbation<sup>24</sup>. The presence of COPD appears in turn to increase the mortality risk in patients with COVID-19. Our data, indicating that COPD is a significant mortality risk factor, are consistent with the results of published studies. In a cohort conducted in Wuhan (n=119; 3% with COPD), non-survivors were more likely to be diagnosed with COPD than survivors (7% vs 1%)<sup>25</sup>. In another Chinese multicenter study, 15.7% of the critically ill COVID-19 patients presented with COPD, but only 2.3% of

those with mild severity disease<sup>26</sup>. Overall, evidence grows stronger for COPD as a risk factor for developing severe COVID-19 disease. Indeed, the presence of COPD tripled the risk of invasive mechanical ventilation, ICU admission, or death in 1590 patients in China (OR=2.681; p=0.002)<sup>27</sup>. Moreover, in another major cohort of 3988 COVID-19 patients, COPD was shown to be an independent risk factor for mortality<sup>17</sup>.

SARS-CoV-2 is similar in triggering pneumonia to SARS-CoV, the agent causing the 2002–2003 SARS pandemic. The cellular serine protease TMPRSS2 activates the spike protein of SARS-CoV-2, present in the virus envelope, facilitating the connection of the virus to the cell's angiotensin converting enzyme 2 (ACE-2) receptor and afterwards follows the entrance to the cell. It has been recently shown that there is a significantly higher expression of ACE-2 in COPD patients than in the control individuals. Although it has not been proven that ACE-2 expression alone confers greater susceptibility or greater severity of the disease<sup>22</sup>, our data seem to underline once again how the presence of COPD can lead to worse COVID-19 outcomes, including mortality. Our data relates to a population enrolled during the entire period of the COVID-19 pandemic, from March 2020 to August 2021, unlike other studies covering shorter periods<sup>17,25,27</sup>; in other words, COPD seemed to maintain its role as a mortality predictor in patients with COVID-19, despite the improvement in the clinical and management knowledge during the pandemic.

Another independent comorbidity in our population that increased the mortality risk was malignancy. Although this finding is not confirmed in some cohort studies<sup>19,28</sup>, it is evident in others. In a retrospective study including 2476 patients (March to May 2020) in Massachusetts, presenting with cancer or CVD doubled the mortality risk in severe COVID-19 patients (HR=2.02; 95% CI: 1.53–2.68, p<0.001; HR=1.79; 95% CI: 1.21–2.66, p=0.004, respectively)<sup>28</sup>. Although prior cardiovascular disease was an independent mortality risk factor in the univariate analysis in our study, it was not confirmed in the multivariate analysis. This could be attributed to the fact that our study took into consideration only the pre-hospitalization characteristics without any clinical data, which may not reveal certain clinically relevant risk factors.

The importance of the presence of CVD in the clinical management of the COVID-19 hospitalized patients is further confirmed by the fact that it is the only independent predictor of a longer hospital stay. The median hospitalization of our population was 11 days. The median duration of hospitalization in other countries ranged 4–21 days outside China and 4–53 days in China<sup>26</sup>. Overall, 15.4% of the patients with a shorter hospitalization than the median were hospitalized during the 4th COVID wave. These data can be plausibly explained by the improvement in the experience of both the administrative and clinical organization. Other studies have also focused on the duration of hospitalization.

A cohort including 100 patients hospitalized in the Pisana University Hospital (Pisa, Italy), between March and April 2020, associated obesity with duration of hospitalization (21 vs 13 days, for obese and non-obese patients, respectively)<sup>29</sup>.

### Limitations

The main limitation of our study is the evaluation of only the baseline demographic characteristics of the patients, without considering any information on the clinical, laboratory or paraclinical parameters during the hospital stay. At the same time, a significant merit is that our analyses were conducted in a large cohort of 627 patients throughout the pandemic period with data that were prospectively collected using a meticulous recording system.

### CONCLUSIONS

The present large cohort conducted in a tertiary COVID-19 referral hospital during the first four waves of the ongoing pandemic period in Greece, shed new light on the role of COPD and malignancy in the mortality risk of patients hospitalized with COVID-19. The presence of cardiovascular disease, on the other hand, appeared to be an independent risk factor for a longer duration of hospital stay among the patients who were subsequently discharged. Future studies are necessary in order to confirm our findings by acquiring information related to the clinical course, laboratory, and radiographic parameters of the patients with COVID-19 admitted to the hospital.

### CONFLICTS OF INTEREST

The authors have each completed and submitted an ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors declare that they have no competing interests, financial or otherwise, related to the current work. K. Kostikas reports that he is the Editor in Chief of the *Pneumon* journal.

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### ETHICAL APPROVAL AND INFORMED CONSENT

This study was approved by the institutional review board of the University Hospital of Ioannina (IRB No. 28/23-05-2021). Informed consent was obtained from all subjects involved in the study.

### DATA AVAILABILITY

The data supporting this research are available from the corresponding author on reasonable request.

### PROVENANCE AND PEER REVIEW

Not commissioned; externally peer reviewed.

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