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Pattern of SARS-CoV-2 infection among dependant elderly residents living in long-term care facilities in Marseille, France, March-June 2020

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Abstract (250/250 words)

Objectives. We aimed to report the results of SARS-CoV-2 PCR-based screening campaigns conducted on dependent elderly residents (compared to staffs members) in long-term care facilities (LTCFs) in Marseille, France, and the follow-up of positive cases.

Methods. Data from 1,691 elderly residents and 1,000 members of staff were retrospectively collected through interviewing the medical teams in 24 LTCFs and using the hospitals' electronic health recording systems.

Results. Elderly residents were predominantly female (64.8%) with a mean age of 83.0 years. SARS-CoV-2 detection among residents (226, 13.4%) was significantly higher than among staff members (87, 8.7%), with p<0.001. Of the 226 infected residents, 37 (16.4%) were detected on a case-by-case basis due to their COVID-19 symptoms and 189 (83.6%) were detected through mass screening. Most (77.0%) had possible COVID-19 symptoms, including respiratory symptoms and signs (44.5%) and fever (46.5%) and 23.0% were asymptomatic. 116 (51.4%) patients received a course of oral hydroxychloroquine and azithromycin (HCQ-AZM) for ≥3 days, and 47 (20.8%) died. Through multivariate analysis, the death rate was positively associated with being male (30.7%, vs. 14.0%, OR=3.95, p=0.002), being older than 85 years (26.1%, vs. 15.6%, OR=2.43, p=0.041), and receiving oxygen therapy (39.0%, vs. 12.9%, OR=5.16, p<0.001) and negatively associated with being diagnosed through mass screening (16.9%, vs. 40.5%, OR=0.20, p=0.001) and receiving HCQ-AZM treatment ≥3 days (15.5%, vs. 26.4%, OR=0.37, p=0.02).

Conclusion. High proportion of asymptomatic COVID-19 patients and independent factors for mortality suggests that early diagnosis and treatment of COVID-19 patients in LTCFs may be effective in saving lives.

Introduction

In France, as of 2 June 2020, 10,350 elderly residents living in long-term care facilities or medical-social establishments had died from COVID-19 (27.6% lethality rate) accounting for 55.6% of COVID-19 deaths in France [1]. Similar pictures have also been reported in many European countries [2] and worldwide [3]. The prevalence of chronic conditions such as cardiovascular diseases, hypertension and diabetes mellitus is high among elderly persons living in long-term care facilities; coronavirus disease (COVID-19) in this population may therefore have severe outcomes with a high mortality rate [2, 4, 5]. Other drivers of mortality among elderly persons living in long-term care facilities already include type of facility, the amount of persons visiting the facilities during the week previous to lockdown, staff ratios [3], and lagged infection in staff members [6].

The treatment of COVID-19 has been the subject of widespread controversy, in particular with regards to the use of hydroxychloroquine (HCQ) [7]. It appears to us that some of the elements of the controversy are the heterogeneity of protocols using HCQ, with doses ranging from 800 mg to 1200 mg per day, the duration of treatment, whether or not it is combined with azithromycin (AZM), and the stage of the disease at which patients were being treated. It can be considered that there is a purely viral phase of the disease with a more or less strong immune response, which can become predominant in what has been referred to as the cytokine storm, followed in a number of cases, by necrotic lesions, linked to pulmonary infarctions [8]. Furthermore, mortality depends very significantly on age and thus, in Europe, almost all deaths have been among persons over the age of 60, with more than 50% in persons over the age of 85 years [9]. Under these conditions, it is very difficult to carry out comparative studies addressing the effect of HCQ on COVID-19-associated deaths. Very few randomised studies have been conducted and their interpretations have also led to heated

89 debate. To assist the debate, we believe that it may be important to assess whether there is a
90 clear reduction in mortality in the most at-risk groups.

91 In Marseille, over a period of approximately two months, we were able to test and treat
92 COVID-19 patients in long-term care facilities (Etablissement d'Hébergement pour Personnes
93 Agées Dépendantes –EHPAD) with a combination of HCQ-AZM, as we have described it on
94 several occasions [8, 10-12]. The objective of this study was to estimate the prevalence of
95 SARS-CoV-2 carriage among elderly residents and among staff members working in 24
96 EHPAD, Marseille, France. We also aimed to estimate the lethality among elderly residents
97 treated in these EHPADs and informally compare it to the lethality of patients in these EHPAD
98 who were not treated s and the general lethality of patients in EHPADs in France.

99 **Methods**

100 **Setting, study design and population**

101 SARS-CoV-2 cross-sectional mass screening campaigns were conducted among residents and
102 staff members from 24 long-term care facilities (EHPADs) in Marseille, between 24 March
103 and 2 June 2020. In some centres, screening campaigns were conducted following the
104 diagnosis of confirmed COVID-19 cases in symptomatic patients who were sampled on a
105 case-by-case strategy. In other centres, screening campaigns were conducted systematically.
106 In all cases, screening campaigns were conducted following a request from the directors and
107 medical staff of the long-term care facilities. Nasopharyngeal samples were processed for
108 SARS-CoV-2 PCR testing at the Institut Hospitalo-Universitaire (IHU) Méditerranée Infection
109 at Assistance Publique-Hôpitaux de Marseille (AP-HM), as previously described [13] or in
110 private laboratories in Marseille, in some cases. Residents who tested positive were either i)
111 treated at their long-term care facilities by local medical staff only, ii) treated at their long-
112 term care facilities in coordination with the AP-HM Home Hospitalisation Unit (HHU), iii)

admitted to the IHU (day-care hospital or conventional units), or iv) transferred to AP-MH Intensive Care Units (ICU). For confirmed cases, information on demographics, chronic medical conditions, COVID-19 treatment and clinical data including fever, asthenia, anorexia and weight loss, respiratory symptoms and signs (cough, rhinorrhoea, dyspnoea, chest pain, acute respiratory distress syndrome) and death was collected retrospectively from interviews with the medical team of 24 long-term care facilities and the electronic health recording systems of the AP-HM.

Statistical methods

Statistical procedures were performed using STATA 11.1. We used Pearson's chi-square or Fisher's exact tests to compare differences between groups of patients where appropriate. A two-sided p-value of less than 0.05 was considered to be statistically significant. A separate logistic regression analysis was used to identify independent risk factors for SARS-CoV-2 death prevalence among all elderly residents testing positive for SARS-CoV-2. The results were presented by percentages and odds ratio (OR) with a 95% confidence interval (95%CI). The initial model included variables presenting a p-value <0.2. The stepwise regression procedure and likelihood-ratio tests were applied to determine the final model.

Results

Over the study period, 1,691 elderly residents and 1,000 staff members were tested (Table 1). For residents, the sex ratio (male to female) was 1:1.8 and the mean age (± standard derivation [SD]) was 83.0 (±10.6) years (ranging from 50 to 106 years). For staff members, the sex ratio was 1:3.5 and the mean age (± SD) was 40.8 (±12.8) years (ranging from 18 to 87 years). It should be noted that two religious staff members at one long-term care facility were aged 75 and 87, respectively.

Overall, 313 participants (of 2,691, 11.6%) were confirmed positive for SARS-CoV-2. The prevalence among residents (226 of 1,691, 13.4%) was significantly higher than among staff members (87 of 1,000, 8.7%), $p<0.001$). With regard to the housing facilities, at least one individual was positive in 11/24 (45.8%) centres with prevalence of SARS-CoV-2 detection ranging from 0% to 57.6% among residents and from 0% to 24.1% among staff members (Table 1). The lethality rate among residents was 20.8% while no deaths occurred among staff members ($p<10^{-4}$).

Characteristics of 226 elderly residents testing positive for SARS-CoV-2 (Tables 2 and 3)

Of the 226 SARS-CoV-2-positive elderly residents, 37 were diagnosed on a case-by-case basis through selected sampling of patients with COVID-19 symptoms and 189 (83.4%) were detected through mass screening. Regarding co-morbidities, the most frequent chronic condition was hypertension (39.6%), followed by other cardiovascular diseases (37.1%), dementia (28.9%) and other mental disorders (23.6%). In terms of clinical findings, 77.0% had possible COVID-19 symptoms, including respiratory symptoms and signs (44.5%), and fever (46.5%); and 23.0% had no COVID-19 symptoms representing 24.8% (40/161) of individuals tested through mass screening (Table 2).

When it came to therapeutic management, 62 (27.4%) patients were managed within their long-term care facilities by local medical staff only, 117 (51.8%) were managed within their long-term care facility in collaboration with the HHU, 16 (7.1%) were admitted to IHU, and 31 (13.7%) were transferred to ICU. Overall, 116 (51.4%) patients received an oral HCQ (200 mg three times daily for ten days), and AZM (500 mg on day 1 followed by 250 mg daily for the next four days) for at least three days and were monitored as described in previous studies [10-12]. Of the 110 others (48.6%), one (0.4%) received a two-day course of HCQ-AZM, one (0.4%) received HCQ alone, 37 (16.4%) received AZM alone, and 71 (31.4) did not receive either drug. The prevalence of HCQ-AZM treatment for at least three days ranged from 0%-

87.5% according to the housing facilities. Other treatments are described in Table 2. A total of 179 patients survived (79.2%) and 47 (20.8%) died.

The baseline characteristics of 116 patients who received HCQ-AZM treatment for at least three days compared with 110 patients who did not receive the treatment were largely similar (Table 3). A higher proportion of patients with a history of stroke was observed in the treated group (15.8%) compared with the untreated group (5.2%, p=0.04).

Table 4 shows the lethality rate among elderly residents with SARS-CoV-2 infection, according to demographics, chronic conditions, circumstance of diagnosis, type of medical management of patients, use of HCQ-AZM and housing facility effect according to prevalence of HCQ-AZM treatment for at least three days in each housing facility. Under univariate analysis, death from COVID-19 was significantly associated with male gender. In addition, patients who were diagnosed on a case-by case basis due to their COVID-19 symptoms were more likely to die (40.5%) than those diagnosed through systematic screening (16.9%). Finally, patients who received oxygen treatment were more likely to die (39.0%) than those who did not receive such a treatment (12.9%), by contract, patients who received HCQ-AZM treatment for at least three days were less likely to die (15.5%) than those who did not receive such a treatment (26.4%). Through multivariate analysis, the death rate was positively associated with being male (30.7% vs. 14.0%, OR=3.95 [1.65-9.44], p=0.002), being older than 85 years (26.1% vs. 15.6%, OR=2.43 [1.04-5.69], p=0.041), and receiving oxygen therapy (OR=5.16 [2.26-11.76], $p<10^{-4}$) and negatively associated with being diagnosed through mass screening (16.9%, vs. 40.5%, OR=0.20 [0.08-0.53], p=0.001) and receiving HCQ-AZM treatment for at least three days (OR=0.37 [0.17-0.86], p=0.02).

Discussion

In Marseille, the first case of COVID-19 in the general population was diagnosed on 3 March 2020 and the epidemic peaked during the first week of April and remained active until the end of the month. Our survey of long-term care facilities began when the entire French population was placed under a strict lockdown (17 March) and when the epidemic was active in Marseille. All long-term care facilities became confined environments with very strict restrictions being place upon visits. We found a 13.4% SARS-CoV-2 positivity rate among dependant elderly residents in Marseille that was significantly higher than the 5.4% positivity rate among all French dependant elderly residents according to a national survey (37,405 confirmed cases in an estimated 695,060 French dependant elderly residents, $p<0.001$, 2 June update) [1, 14]. We observed an overall 20.8% COVID-19 lethality rate among infected residents in Marseille that was significantly lower than that in all French long-term care facilities or medical-social establishments (27.7% lethality rate, $p=0.026$, 2 June update) [1]. The main drivers of mortality in Marseille residents were older age and male sex, as already reported in many studies [15]. In addition, systematic screening by PCR was identified as an independent protective factor against death from COVID-19. A symptom-based diagnostic strategy is less effective in long-term care facilities, most likely because elderly patients with comorbidities such as chronic respiratory or cardiovascular diseases may be unable to accurately report new symptoms suggestive of COVID-infection or may present with atypical symptoms that challenge medical staff [13, 17]. Furthermore, in our experience, more than 23% of SARS-CoV-2 infected residents had no symptoms at the time of sampling. A very high prevalence (around 80%) was observed in a cross-sectional study conducted on elderly residents living in 2074 Belgian long-term care facilities [18]. In this study, we show that there was a significant difference in lethality between patients treated with our standardised treatment and untreated patients, as already reported in study conducted among elderly patients living in a Spanish

public nursing home in the same period [14]. Treatment with HCQ alone was demonstrated to be associated with lower mortality in patients admitted with COVID-19 [20-23]. Another cohort study conducted among American patients with rheumatic conditions showed an association between long-term HCQ treatment and reduced COVID-19 lethality rate [24]. The potential mechanisms of HCQ in the decrease of mortality in COVID-19 might be its inhibitory effects upon the production of pro-inflammatory cytokines interleukin (IL)-1-β, TNF-α and IL-6, and chemokines (CCL2 and CCL3) involved in the recruitment of pro-inflammatory cells in the lung [25].

There are some limitations to our study. Our study population was not randomly and homogenously recruited. Data regarding demographics, chronic conditions and clinical status was not systematically documented. Frailty that has been shown to be a major risk factor for mortality in COVID-19 was not evaluated in this study due to its retrospective design [26]. The use of individual preventive measures was not documented.

Nevertheless, we believe that even if there are biases, as in any comparative study including randomisation, these biases are relatively neutralised by the multifactorial study. Above all, we demonstrate that the mortality in patients treated in EHPADs in Marseille was half that of patients in nursing homes across France who, in most cases very likely did not receive specific treatment since its use is restricted to the hospital setting [27, 28]. We believe that focusing on the population with the highest mortality, to show a significant effect, is important and agree in this sense with several studies that have shown a reduction in mortality of 30 to 50% by HCQ-AZM in populations most at risk [29, 8].

Declarations

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Competing Interests. No potential conflict of interest relevant to this article was reported.

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Writing – original draft: TD, PG

Writing – review & editing: TD, DZ, VL, SA, SG, HM, MF, DM, OQ, PM, AM, PL, GD, BL, AM, AC, PA, PP, EC & DR

Conceptualization: PG

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360 **Table 1.** SARS-CoV-2 testing among residents and staff members at 24 long-term care
361 facilities in Marseille, France, 27 March– 2 June 2020

362 **Table 2.** Comorbidities, symptoms and signs, diagnostic and therapeutic management among 226
363 elderly residents testing positive for SARS-CoV-2.

364 **Table 3.** Characteristics of group receiving HCQ-AZ for at least 3 days and untreated group.

365 **Table 4.** Associations between multiple factors and SARS-CoV-2 deaths among 226 infected
366 elderly residents (univariate and multivariate analysis)

367

Table 1. SARS-CoV-2 testing among residents and staff members at 24 long-term care facilities in Marseille, France, 27 March– 2 June 2020

Characteristics	Residents				Staff members			p-value[1]	p-value[2]	Total	
	Date of mass testing	No. tested	No. (%) positive	No. (%) deaths among positive cases (lethality rate)	No. tested	No. (%) positive	No. (%) deaths among positive cases (lethality rate)			No. tested	No. (%) positive
Total		**1691**	**226 (13.4)**	**47 (20.8)**	**1000**	**87 (8.7)**	**0 (0)**	**4.10^{-4}**	**$<10^{-4}$**	**2691**	**313 (11.6)**
Centre (2691)											
Centre-01	01 April, 08 April, 19 April	99	57 (57.6)	17 (29.9)	83	20 (24.1)	0 (0)	2.10^{-3}	0.04	182	77 (42.3)
Centre-02	08 April, 19 April, 20 May	112	50 (44.6)	9 (18.0)	71	17 (24.0)	0 (0)	7.10^{-3}	0.053	183	67 (36.6)
Centre-03	20 April, 26 April, 04 May, 11 May, 18 May, 25 May, 02 June	52	23 (44.2)	2 (8.7)	35	7 (20.0)	0 (0)	2.10^{-3}	N/A	87	30 (34.5)
Centre -04	06 April, 21 April	89	24 (27.0)	8 (33.3)	108	12 (11.1)	0 (0)	7.10^{-3}	0.03	197	36 (18.3)
Centre -05	08 April, 29 April	37	10 (27.1)	3 (30.0)	32	1 (3.1)	0 (0)	0.035	N/A	69	11 (16.0)
Centre -06	08 April, 17 April, 22 April	230	45 (18.0)	7 (15.6)	180	15 (8.3)	0 (0)	2.10^{-3}	0.18	410	60 (14.9)
Centre -07	02 Avril, 27 April, 25 May	81	8 (9.9)	0 (0)	57	11 (19.3)	0 (0)	0.18	N/A	138	19 (13.8)
Centre -08	13 April, 06 May	77	7 (9.1)	1 (14.3)	24	1 (4.2)	0 (0)	0.67	N/A	101	8 (7.9)
Centre -09	21 April	54	0 (0)	N/A	44	3 (6.8)	0 (0)	0.08	N/A	98	3 (3.1)
Centre -10	23 April	46	1 (2.2)	0 (0)	12	0 (0)	N/A	N/A	N/A	58	1 (1.7)
Centre -11	15 April	118	1 (0.9)	0 (0)	60	0 (0)	N/A	N/A	N/A	178	1 (0.6)

Centre -12	15 April	66	0 (0)	N/A	18	0 (0)	N/A	N/A	N/A	84	0 (0)
Centre -13	28 April	96	0 (0)	N/A	39	0 (0)	N/A	N/A	N/A	135	0 (0)
Centre -14	30 April	45	0 (0)	N/A	12	0 (0)	N/A	N/A	N/A	57	0 (0)
Centre -15	17 April	64	0 (0)	N/A	27	0 (0)	N/A	N/A	N/A	91	0 (0)
Centre -16	22 April	48	0 (0)	N/A	19	0 (0)	N/A	N/A	N/A	67	0 (0)
Centre -17	25 April	61	0 (0)	N/A	29	0 (0)	N/A	N/A	N/A	90	0 (0)
Centre -18	15 April	52	0 (0)	N/A	18	0 (0)	N/A	N/A	N/A	70	0 (0)
Centre -19	27 April	32	0 (0)	N/A	24	0 (0)	N/A	N/A	N/A	56	0 (0)
Centre -20	27 April	29	0 (0)	N/A	15	0 (0)	N/A	N/A	N/A	44	0 (0)
Centre -21	24 April	25	0 (0)	N/A	11	0 (0)	N/A	N/A	N/A	36	0 (0)
Centre -22	20 April	53	0 (0)	N/A	22	0 (0)	N/A	N/A	N/A	75	0 (0)
Centre -23	14 April	100	0 (0)	N/A	52	0 (0)	N/A	N/A	N/A	152	0 (0)
Centre -24	24 April	25	0 (0)	N/A	8	0 (0)	N/A	N/A	N/A	33	0 (0)
Sex (2471)											
Female, n (%)		1,069 (64.8)	135 (12.6)	19 (14.1)	646 (77.7)					1705 (69.0)	
Male, n (%)		581 (35.2)	91 (15.7)	28 (30.8)	185 (22.3)					766(31.0)	
Age (years) (2556)											
Mean±SD		83.0±10.6	83.4±10.6	86.8±10.2	40.8±12.7					68.3±23.1	
Range (min-max)		50-106	56-103	59-103	18-87					18-106	
18-34,n (%)		0 (0)	N/A	N/A	326 (36.4)					326 (12.8)	
35-49, n (%)		0 (0)	N/A	N/A	292 (32.6)					292 (11.4)	
50-59, n (%)		34 (2.1)	3 (8.8)	1 (33.3)	236 (25.4)					270 (10.6)	
60-69, n (%)		189 (11.4)	25 (13.2)	3 (12.0)	38 (4.2)					227 (8.9)	
70-79, n (%)		348 (21.0)	46 (13.2)	5 (10.9)	1 (0.1)					349 (13.7)	
80-89, n (%)		552 (33.2)	78 (14.1)	16 (20.5)	1 (0.1)					553 (21.6)	
90-99, n (%)		505 (30.3)	67 (13.3)	19 (28.4)	0 (0)					505 (19.8)	
>99, n (%)		34 (2.1)	7 (20.6)	3(42.9)	0 (0)					34 (1.3)	

Abbreviation: N/A, not applicable;

[1]Comparison of positive testing prevalence between resident group and staff member group.

[2]Comparison of lethality rates between infected resident group and infected staff member group.

[3] Number of individuals for whom data was available.

Table 2. Comorbidities, symptoms and signs, diagnostic and therapeutic management among 226 elderly residents testing positive for SARS-CoV-2.

Parameters	n (%)
Comorbidities (159) [1]	
Hypertension	63 (39.6)
Cardiovascular diseases (other than hypertension)	59 (37.1)
Dementia	46 (28.9)
Mental disorder	39 (23.6)
Diabetes mellitus	25 (15.7)
Chronic lung diseases	19 (12.0)
Stroke	17 (10.7)
Cancer	15 (9.4)
Chronic neurological disorder	12 (7.6)
Obesity	7 (4.4)
Chronic kidney diseases	7 (4.4)
Asthma	3 (1.9)
Symptoms and signs (200)	
Respiratory symptoms and signs	89 (44.5)
Fever	93 (46.5)
Asthenia, anorexia, weight loss	21 (10.5)
No COVID-19 symptoms	46 (23.0)
Circumstances of diagnosis (226)	
Case-by-case testing in patients with COVID-19 symptoms	37 (16.4)
Mass testing	189 (83.6)
Medical management of patients (226)	
Managed at long-term care facilities by local medical staff only	62 (27.4)
Managed at long-term care facilities in coordination with the HHU	117 (51.8)

	Admitted to IHU	16 (7.1)
	Transferred ICU	31 (13.7)
HCQ-AZM therapy (226)		
	At least a three-day course	116 (51.4)
	two-day course	1 (0.4)
	HCQ alone	1 (0.4)
	AZM alone	37 (16.4)
	No HCQ, no AZM	71 (31.4)
HCQ-AZM therapy at least a three-day course according to the housing facilities (226)		
	Centre-07, n/N (%)	7/8 (87.5)
	Centre-01, n/N (%)	39/50 (78.0)
	Centre-02, n/N (%)	43/57 (75.4)
	Centre -05, n/N (%)	4/10 (40.0)
	Centre -06, n/N (%)	14/45 (31.1)
	Centre -04, n/N (%)	4/23 (17.3)
	Centre -03, n/N (%)	4/24 (16.7)
	Centre -08, n/N (%)	1/7 (14.3)
	Centre -10, n/N (%)	0/1 (0)
	Centre -11, n/N (%)	0/1 (0)
Oxygen therapy (199)		59 (29.7)
Ceftriaxone or ertapenem therapy (199)		63 (31.6)
Low-molecular-weight heparin therapy (199)		24 (12.1)

Abbreviation: HCQ, hydroxychloroquine; AZM, azithromycin; HHU, Home Hospitalisation Unit, Institut Hospitalo-Universitaire; ICU, Intensive Care Units.

[1] Number of individuals for whom data was available.

Table 3. Characteristics of group receiving HCQ-AZ for at least 3 days and untreated group.

Characteristics		Patient receiving HCQ-AZ ≥3 days N=116	Patient not receiving HCQ-AZ ≥3 days N=110	p-value
Demographic factors (226) [1]				
Gender	Female, n (%)	70 (60.3)	65 (59.1)	0.85
	Male, n (%)	46 (39.7)	45 (40.9)	
Age (years)[2]	50-85, n (%)	66 (56.9)	49 (44.5)	0.07
	>85, n (%)	50 (43.1)	61 (55.5)	
Chronic conditions (159)				
Cardiovascular diseases	No, n (%)	51 (62.2)	49 (63.6)	0.85
	Yes, n (%)	31 (37.8)	28 (36.4)	
Hypertension	No, n (%)	46 (56.1)	50 (64.9)	0.26
	Yes, n (%)	36 (43.9)	27 (35.1)	
Dementia	No, n (%)	61 (74.4)	52 (67.5)	0.34
	Yes, n (%)	21 (25.6)	25 (32.5)	
Mental disorder	No, n (%)	61 (74.4)	59 (76.6)	0.74
	Yes, n (%)	21 (25.6)	18 (23.4)	
Diabetes mellitus	No, n (%)	69 (84.1)	65 (84.4)	0.96
	Yes, n (%)	13 (15.9)	12 (15.6)	
Chronic lung diseases	No, n (%)	72 (87.8)	68 (88.3)	0.92
	Yes, n (%)	10 (12.2)	9 (11.7)	

Stroke	No, n (%)	69 (84.2)	73 (94.8)	0.04
	Yes, n (%)	13 (15.8)	4 (5.2)	
Cancer	No, n (%)	74 (90.2)	70 (90.9)	0.86
	Yes, n (%)	8 (9.8)	7 (9.1)	
Chronic neurological disorder	No, n (%)	76 (92.7)	71 (92.2)	0.9
	Yes, n (%)	6 (7.3)	6 (7.8)	
Circumstances of diagnosis (226)	Case-by-case testing in patients with COVID-19 symptoms, n (%)	23 (19.8)	14 (12.7)	0.1
	Mass testing, n (%)	93 (80.2)	96 (87.3)	
Facility management of patients (226)[3]	In long-term care facilities only	0 (0)	62 (56.4)	N/A
	Other	116 (100)	48 (43.7)	
Oxygen therapy (199)	No, n (%)	79 (68.1)	61 (73.5)	0.4
	Yes, n (%)	37 (31.9)	22 (26.5)	
Ceftriaxone or ertapenem therapy (199)	No, n (%)	81 (69.8)	55 (66.3)	0.59
	Yes, n (%)	35 (30.2)	28 (33.7)	
Low-molecular-weight heparin therapy (199)	No, n (%)	98 (84.5)	77 (92.8)	0.08
	Yes, n (%)	18 (15.5)	6 (7.2)	

Abbreviation: HCQ, hydroxychloroquine; AZM, azithromycin; NA, Not applicable.

[1] Number of individuals for whom data was available.

[2] Median of the variable is used for analysis.

[3] Indication of HCQ-AZ treatment was compulsorily administrated in coordination with hospital.

Table 4. Associations between multiple factors and SARS-CoV-2 deaths among 226 infected elderly residents (univariate and multivariate analysis)

Characteristics		Deaths N=47	Survivors N=179	Univariate		Multivariate	
				OR [95%CI]	p-value	aOR [95%CI]	p-value
Demographic factors (226) [1]							
Gender	Female, n (%)	19 (14.0)	116 (86.0)	Ref		Ref	
	Male, n (%)	28 (30.7)	63 (69.2)	**2.71 [1.40-5.24]**	**0.003**	**3.95 [1.65-9.44]**	**0.002**
Age (years)[2]	50-85, n (%)	18 (15.6)	97 (84.4)	Ref		Ref	
	>85, n (%)	29 (26.1)	82 (73.9)	**1.90 [0.99-3.67]**	**0.055**	**2.43 [1.04-5.69]**	**0.041**
Chronic conditions (159)							
Cardiovascular diseases	No, n (%)	21 (21.0)	79 (79.0)	Ref			
	Yes, n (%)	12 (20.3)	47 (79.7)	0.98 [0.43-2.12]	0.92		
Hypertension	No, n (%)	23 (24.0)	73 (76.0)	Ref			
	Yes, n (%)	10 (15.9)	53 (84.1)	0.59 [0.26-1.36]	0.22		
Dementia	No, n (%)	28 (24.8)	85 (75.2)	Ref			
	Yes, n (%)	5 (10.9)	41 (89.1)	**0.37[0.13-1.02]**	**0.057**		
Mental disorder	No, n (%)	25 (20.9)	95 (79.1)	Ref			
	Yes, n (%)	8 (20.5)	31 (79.5)	0.98 [0.40-2.39]	0.96		
Diabetes mellitus	No, n (%)	27 (20.2)	107 (79.8)	Ref			
	Yes, n (%)	6 (24.0)	19 (76.0)	1.25 [0.45-3.43]	0.66		
Chronic lung	No, n (%)	26 (18.6)	114 (81.4)	Ref			

diseases	Yes, n (%)	7 (36.9)	12 (63.1)	**2.55 [0.91-7.12]**	**0.073**		
Stroke	No, n (%)	31 (21.8)	11 (78.2)	Ref			
	Yes, n (%)	2 (11.7)	15 (88.3)	0.47 [0.1-2.20]	0.34		
Cancer	No, n (%)	28 (19.4)	116 (80.6)	Ref			
	Yes, n (%)	5 (33.3)	10 (66.7)	2.07 [0.65-6.54]	0.215		
Chronic neurological disorder	No, n (%)	30 (20.4)	117 (79.6)	Ref			
	Yes, n (%)	3 (25.0)	9 (75.0)	1.30 [0.33-5.10]	0.71		
Diagnostic and therapeutic management factors							
Circumstances of diagnosis **(226)**	Case-by-case testing in patients with COVID-19 symptoms, n (%)	15 (40.5)	22 (59.5)	Ref		Ref	
	Mass testing, n (%)	32 (16.9)	157 (83.1)	**0.30 [0.14-0.64]**	**0.002**	**0.20 [0.08-0.53]**	**0.001**
Facility management of patients **(226)**	In long-term care facilities only	12 (19.4)	50 (80.3)	Ref			
	Other	35 (21.3)	129 (78.7)	1.13 [0.54-2.35]	0.74		
HCQ-AZM treatment for at least three days **(226)**	No, n (%)	29 (26.4)	81 (73.6)	Ref		Ref	
	Yes, n (%)	18 (15.5)	98 (84.5)	**0.51 [0.26-0.99]**	**0.047**	**0.37 [0.17-0.86]**	**0.02**
Housing facility effect[3] (226)	>75%	26 (22.6)	89 (77.4)	Ref			
	25%-75%	11 (20.0)	44 (80.0)	0.85 [0.38-1.89]	0.7		
	<25%	10 (17.9)	46 (82.1)	0.74 [0.33-1.67]	0.48		
Oxygen therapy **(199)**	No, n (%)	18 (12.9)	122 (87.1)	Ref		Ref	
	Yes, n (%)	23 (39.0)	36 (61.0)	**4.33 [2.1-8.89]**	**$<10^{-4}$**	**5.16 [2.26-11.76]**	**$<10^{-4}$**
Ceftriaxone or	No, n (%)	26 (19.1)	110 (80.9)	Ref			

ertapenem therapy **(199)**	Yes, n (%)	15 (23.8)	48 (76.2)	1.32 [0.64-2.71]	0.45
Low-molecular-weight heparin therapy **(199)**	No, n (%)	36 (20.6)	139 (79.4)	Ref	
	Yes, n (%)	5 (20.8)	19 (79.2)	1.01 [0.35-2.90]	0.97

Abbreviation: Ref, Reference; NA, Not applicable; OR, Odds-ratio; aOR, adjusted Odds-ratio; HCQ, hydroxychloroquine; AZM, azithromycin

[1] Number of individuals for whom data was available.

[2] Median of the variable is used for analysis.

[3] According to prevalence of HCQ-AZM treatment for at least three days among infected residents in each housing facility as seen in Table 2.

Bold lines indicate the variables recruited in initial multivariate mode.