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Research Article

Clinical Features and Risk Factors for Mortality Among Long-term Care Facility Residents Hospitalized Due to COVID-19 in Spain

José-Manuel Ramos-Rincón, MD, PhD,[1,*] Máximo Bernabeu-Wittel, MD, PhD,[2,3] Isabel Fiteni-Mera, MD, PhD,[4] Almudena López-Sampalo, MD,[5] Carmen López-Ríos, MD,[2] María-del-Mar García-Andreu, MD,[4] Juan-José Mancebo-Sevilla, MD,[5] Carlos Jiménez-Juan, MD,[2] Marta Matía-Sanz, MD,[4] Pablo López-Quirantes, MD,[5] Manuel Rubio-Rivas, MD, PhD,[6] Diana Paredes-Ruiz, MD,[7] Candela González-San-Narciso, MD,[8] Rocío González-Vega, MD,[9] Pablo Sanz-Espinosa, MD,[10] Almudena Hernández-Milián, MD,[11] Amara Gonzalez-Noya, MD,[12] Ricardo Gil-Sánchez, MD,[13] Ramon Boixeda, MD,[14] José-Nicolás Alcalá-Pedrajas, MD,[15] Marta Palop-Cervera, MD,[16], Begoña Cortés-Rodríguez, MD,[17] María-Esther Guisado-Espartero, MD,[18] Carmen Mella-Pérez, MD,[19] and Ricardo Gómez-Huelgas, MD, PhD,[5,20] for the SEMI-COVID-19 Network[**]

[1]Clinical Medicine Department, Miguel Hernandez University of Elche, Alicante, Spain. [2]Internal Medicine Department, Virgen del Rocío University Hospital, Seville, Spain. [3]Medicine Department, University of Seville, Sevilla, Spain. [4]Internal Medicine Department, Royo Villanova Hospital, Zaragoza, Spain. [5]Internal Medicine Department, Málaga Regional University Hospital- Biomedical Research Institute of Málaga (IBIMA), Málaga, Spain. [6]Internal Medicine Department, Bellvitge University Hospital- -IDIBELL, L'Hospitalet de Llobregat (Barcelona), Spain. [7]Internal Medicine Department, 12 Octubre University Hospital, Madrid, Spain. [8]Internal Medicine Department, Gregorio Marañon University Hospital, Madrid, Spain. [9]Internal Medicine Department, Costa del Sol Hospital, Marbella (Malaga), Spain. [10]Internal Medicine Department, Rio Hortega University Hospital, Valladolid, Spain. [11]Internal Medicine Department, Son Llàtzer University Hospital, Palma de Mallorca, Spain. [12]Internal Medicine Department, Ourense University Hospital Complex, Ourense, Spain. [13]Internal Medicine Department, La Fe University Hospital, Valencia, Spain. [14]Internal Medicine Department, Mataró Hospital, Mataró (Barcelona), Spain. [15]Internal Medicine Department, Pozoblanco Hospital, Pozoblanco (Cordoba), Spain. [16]Internal Medicine Department, Sagunto University Hospital, Sagunto (Valencia), Spain. [17]Internal Medicine Department, Alto Guadalquivir Hospital, Andújar (Jaén), Spain. [18]Internal Medicine Department, Infanta Margarita Hospital, Cabra (Córdoba), Spain. [19]Internal Medicine Department, Ferrol University Hospital Complex, (Ferrol) A Coruna, Spain. [20]Medicine Department, University of Malaga, Malaga, Spain.

*Address correspondence to: Jose-Manuel Ramos-Rincón, MD, PhD, Department of Clinical Medicine, Miguel Hernandez University of Elche, Cra N332 s/nn, 03550 Sat Joan d'Alacant, Alicante, Spain. E-mail: jose.ramosr@umh.es

**A complete list of the SEMI-COVID-19 Network members is provided in the Supplementary Appendix.

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Abstract

Background: COVID-19 severely impacted older adults and long-term care facility (LTCF) residents. Our primary aim was to describe differences in clinical and epidemiological variables, in-hospital management, and outcomes between LTCF residents and community-dwelling

older adults hospitalized with COVID-19. The secondary aim was to identify risk factors for mortality due to COVID-19 in hospitalized LTCF residents.

Methods: This is a cross-sectional analysis within a retrospective cohort of hospitalized patients ≥75 years with confirmed COVID-19 admitted to 160 Spanish hospitals. Differences between groups and factors associated with mortality among LTCF residents were assessed through comparisons and logistic regression analysis.

Results: Of 6 189 patients ≥75 years, 1 185 (19.1%) were LTCF residents and 4 548 (73.5%) were community-dwelling. LTCF residents were older (median: 87.4 vs 82.1 years), mostly female (61.6% vs 43.2%), had more severe functional dependence (47.0% vs 7.8%), more comorbidities (Charlson Comorbidity Index: 6 vs 5), had dementia more often (59.1% vs 14.4%), and had shorter duration of symptoms (median: 3 vs 6 days) than community-dwelling patients (all, $p < .001$). Mortality risk factors in LTCF residents were severe functional dependence (adjusted odds ratios [aOR]: 1.79; 95% confidence interval [CI]: 1.13–2.83; $p = .012$), dyspnea (1.66; 1.16–2.39; $p = .004$), $SatO_2$ < 94% (1.73; 1.27–2.37; $p = .001$), temperature ≥ 37.8°C (1.62; 1.11–2.38; $p = .013$); qSOFA index ≥ 2 (1.62; 1.11–2.38; $p = .013$), bilateral infiltrates (1.98; 1.24–2.98; $p < .001$), and high C-reactive protein (1.005; 1.003–1.007; $p < .001$). In-hospital mortality was initially higher among LTCF residents (43.3% vs 39.7%), but lower after adjusting for sex, age, functional dependence, and comorbidities (aOR: 0.74, 95%CI: 0.62–0.87; $p < .001$).

Conclusion: Basal functional status and COVID-19 severity are risk factors of mortality in LTCF residents. The lower adjusted mortality rate in LTCF residents may be explained by earlier identification, treatment, and hospitalization for COVID-19.

Keywords: COVID-19, Epidemiology, Mortality, Nursing homes, Risk factors

Older adults are at highest risk of complications and death due to COVID-19, with a mortality rate as high as 50% in hospitalized patients over 80 years of age (1,2). Multimorbidity, functional status, dementia, and frailty are prognostic markers of mortality of COVID-19 in older adults (3,4). The World Health Organization (WHO) classified residents in long-term care facilities (LTCF), whose residents are usually older adults, as a high-risk population during the COVID-19 pandemic and specific guidelines for infection prevention and control among these individuals have been published (5). Nonetheless, large COVID-19 outbreaks with high number of casualties have been reported in care facilities all over the world. This fact has raised the concern of healthcare professionals, scientific societies, and citizens' associations (5–9). In Spain, the mortality rate among LTCF residents with confirmed COVID-19 was 22% (10), and it has been estimated that deaths in these institutions represent 47%–50% of all fatalities during the first wave of COVID-19 in Spain, which lasted from March 1 to June 30, 2020 (11).

To date, a few studies have focused on the clinical characteristics (12,13) and prognostic factors of adverse outcomes (3,13) in older adults hospitalized due to COVID-19 acquired in LTCF. However, few studies have compared the clinical and prognostic differences between older patients hospitalized for COVID-19 admitted from LTCF and those who live in the community (13). The main aim of this study was to analyze the differences in clinical and epidemiological variables, in-hospital management, and outcomes between LTCF residents and community-dwelling older adults hospitalized due to COVID-19 in order to detect potential differences in risk factors and mortality. The secondary aim was to analyze risk factors at admission associated with in-hospital mortality among LTCF residents.

Materials and Methods

Study Design and Population

We conducted a cross-sectional analysis on subjects included in a retrospective, observational, multicenter, nationwide cohort of patients ≥ 75 years of age hospitalized with COVID-19 in Spain from March 1 to June 30, 2020. All patient data were obtained from the Spanish Society of Internal Medicine's SEMI-COVID-19 Registry, which had the participation of 160 Spanish hospitals. The SEMI-COVID-19 Registry prospectively compiles data on the index admission of patients ≥18 years of age with COVID-19 confirmed microbiologically through a reverse transcription polymerase chain reaction (RT-PCR) or antigen test. The database includes around 300 variables that were retrospectively collected after patient discharge. The parameters are grouped under various headings: inclusion criteria, epidemiological data, RT-PCR and serology data, prior comorbidities, medication history, symptoms and physical examination at admission, laboratory (blood gases, metabolic panel, complete blood count, coagulation) and diagnostic imaging tests at admission, additional data at 7 days after admission, pharmacological treatment during the hospitalization, ventilation support, complications during the hospitalization, and progress after discharge and/or 30 days from diagnosis. Patients were treated as per the attending physician's discretion according to local protocols and clinical judgment. More in-depth information on the justification, objectives, methodology, and preliminary results of the SEMI-COVID-19 Registry have recently been published (2,4).

Definition of Variables

Two subgroups were defined within the older adult population according to their care needs prior to admission: (a) LTCF residents and (b) community-dwelling older adults (including those receiving at-home care).

The duration of symptoms (including dyspnea, cough, fatigue, anorexia, diarrhea, and vomiting) was measured as the time between the date of onset of symptoms and the date of hospital admission. To assess pre-admission functional status, we used the Barthel Index (independent or mild functional dependence: 100-91; moderate functional dependence: 90-61; and severe functional dependence: ≤60) (14). The Barthel Index assessment was performed by the patient's attending physician, who inquired about the patient's baseline functional status 2 weeks before hospital admission either with the patient directly or his/her caregivers. Comorbidities were evaluated by means of the age-adjusted Charlson Comorbidity Index (CCI) (15). Atrial fibrillation and heart failure were classified as non-atherosclerotic heart disease. Patients were classified as having dyslipidemia, diabetes mellitus, or hypertension if they had a previous diagnosis on their medical chart or received pharmacological treatment for these conditions. The diagnosis of dementia was also determined based on

patients' electronic medical records. Atherosclerotic cardiovascular disease was established as a medical history of coronary heart disease (myocardial infarction, acute coronary syndrome, angina, or coronary revascularization), cerebrovascular disease (stroke, transient ischemic attack), or peripheral arterial disease (intermittent claudication, revascularization, lower limb amputation, or abdominal aortic aneurysm). Chronic pulmonary disease was defined as an asthma and/or chronic obstructive pulmonary disease diagnosis. Malignancy encompassed hematologic neoplasia and/or solid tumors (excluding non-melanoma skin cancer). The quick sequential organ failure assessment (qSOFA) scale was classified as positive when 2 of the 3 variables (systolic blood pressure <100 mmHg, respiratory rate ≥22 brpm, altered mental status) were met, according to the Sepsis-3 definition. All baseline comorbidities were gathered from patients' electronic medical records obtained from the hospitals. Analytical tests (blood gases, coagulation, metabolic panel, complete blood count) and diagnostic imaging tests were performed at admission.

Complications during the hospitalization were defined pre hoc and were collected from the online electronic data capture system. Ventilatory support included invasive and noninvasive mechanical ventilation and high-flow oxygen therapy (16).

In-hospital mortality (IHM) was the primary outcome variable. More in-depth information about the definition of other variables is available in manuscripts recently published by the SEMI-COVID-19 Network (2,4).

Statistical Analysis

First, differences in clinical and epidemiological variables according to residence (LTCF residents vs community-dwelling individuals) were explored. Second, the differences between non-survivor and survivor LTCF residents were examined. Missing data were excluded from statistical analysis.

The characteristics of each group were analyzed using descriptive statistics. Continuous and categorical variables were expressed as medians and interquartile ranges (IQR) and as absolute values and percentages, respectively. The differences between groups were analyzed using the Mann–Whitney *U* test for continuous variables and Pearson's chi-square test for categorical variables. Statistically significance was defined as $p < .05$.

The differences between the 2 groups (LTCF residents vs community-dwelling individuals) in regard to treatment, complications, and outcomes were adjusted by sex, age, functional dependence, and comorbidities (hypertension, dyslipidemia, non-atherosclerotic heart diseases, atherosclerotic cardiovascular diseases, dementia, diabetes mellitus, chronic pulmonary disease, malignancy, and chronic kidney disease) using a multivariable regression analysis. These values were expressed as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

In the analysis of IHM and complications associated with IHM in LTCF residents, statistically significant variables identified in the univariate analysis ($p < .05$) were entered into a multivariable logistic regression using a stepwise forward selection method with the likelihood ratio test. Model validity was evaluated using the Hosmer–Lemeshow test for estimating goodness of fit to the data and its discriminatory ability using area under the curve (AUC). As some variables were missing, those which were not available for >25% of patients were excluded from the analysis. These included serum ferritin, D-dimer, interleukin-6, procalcitonin, venous lactate, and aspartate aminotransferase. Variables included as part of composite scores, such as the qSOFA model, that were missing for >25% of subjects were also excluded. These included tachypnea (≥20 breaths per minute), hypotension (systolic blood pressure <100 mmHg), and confusion. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (Armonk, NY: IBM Corp). Code and data are available upon reasonable request.

Ethical Aspects

The STROBE statement guidelines were adhered to in the execution and reporting of the study (Supplementary Material). All the patients gave informed consent. When there were biosafety concerns and/or if the patient had been discharged, oral informed consent was obtained and indicated on their charts. In the event the patient had cognitive impairment, informed consent was requested from his/her legal representative. In this work, all data collected, processed, and analyzed were anonymized and used only for the purposes of this project. All data were protected in accordance with the European Union Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data. All authors declared no conflicts of interest in regard to this work. This study was approved by the Institutional Research Ethics Committees of each participating hospital.

Results

Of the 17 122 patients diagnosed with COVID-19 included in the SEMI-COVID-19 Registry, 6 189 were ≥75 years of age. Of them, 456 acquired the disease nosocomially and were excluded. Of the remaining 5 733 patients evaluated, 1 185 (20.7%) were LTCF residents and 4 548 (79.3%) were community-dwelling older adults (Supplementary Figure 1).

Comparison Between LTCF Residents and Community-dwelling Older Adults

LTCF residents were older (median age: 87.4 vs 82.1 years; $p < .001$); predominantly female (61.6% vs 43.2%; $p < .001$); had more moderate-severe functional dependence (82.6% vs 23.8%; $p < .001$); and had more comorbidities (median CCI: 6 vs 5; 82.6% vs 23.8%; $p < .001$), especially dementia (59.1% vs 14.4%; $p < .001$) and cardiovascular disease (31.9% vs 26.6%; $p < .0001$). LTCF residents also had lower rates of dyslipidemia, chronic pulmonary disease, and malignancy (Table 1).

The duration of symptoms was significantly shorter among LTCF residents than community-dwelling older adults (median number of days: 3.0 vs 6.0; $p < .0001$). They presented with dyspnea more often (64.6% vs 58.5%; $p < .001$), but cough, fatigue, anorexia, and diarrhea less often. Compared to community-dwelling older adults, a higher proportion of LTCF residents presented with confusion (44.1% vs 19.3%; $p < .001$), qSOFA index ≥2 (27.3% vs 11.9%; $p < .001$), and pulmonary rales (44.8% vs 37.7%; $p < .001$) upon admission, but a lower proportion had tachypnea (22.1% vs 19.6%; $p < .001$; Table 1). At admission, more LTCF residents had normal chest x-rays (27.1% vs 12.9%) and fewer had bilateral infiltrates (52.2% vs 68.6%; $p < .001$). They also had higher median levels of leukocytes, neutrophils, glucose, and D-dimer as well as lower values of the PO_2/FiO_2 ratio, estimated glomerular filtration rate, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, and ferritin (Table 1).

During hospitalization, more LTCF residents had acute kidney failure (25.6% vs 21.2%; $p = .001$) and pneumonia (18.3% vs

12.8; $p = .001$), but fewer developed severe acute respiratory distress syndrome (ARDS) (20.0% vs 27.0%; $p < .001$). Fewer LTCF residents received in-hospital systemic corticosteroids (35.6% vs 40.5; $p = .002$), tocilizumab (1.7% vs 6.2%; $p < .001$), low-molecular-weight heparin (78.5% vs 83.6%; $p < .001$), and ventilatory therapy (high-flow nasal cannula oxygen, noninvasive

Table 1. Clinical, Radiological, and Analytic Findings at Admission in Patients ≥ 75 y of Age Hospitalized with COVID-19 Living in LTCF

	Missing values	LTCF (n = 1 185)	Community-dwelling (n = 4 548)	p value
Age, median (IQR), years	0	**87.4 (83.5–91.16)**	**82.1 (78.1–86.7)**	**<.001**
Sex, Male	4	**455 (38.4)**	**2 583 (56.8)**	**<.001**
Degree of functional dependence	93			
Independent or mild		204 (17.4)	3 408 (76.2)	**<.001**
Moderate		**416 (35.6)**	**715 (16.6)**	**<.001**
Severe		**550 (47.0)**	**347 (7.8)**	**<.001**
Comorbidities				
CCI, median (IQR)	163	**6 (5-7)**	**5 (4-6)**	**<.001**
Hypertension	12	876 (74.0)	3 353 (73.9)	.94
Dyslipidemia	20	**528 (44.7)**	**2 380 (52.5)**	**<.001**
Non-atherosclerotic heart diseases*	19	**380 (32.1)**	**1 234 (27.2)**	**.001**
Atherosclerotic cardiovascular diseases†	39	**375 (31.9)**	**1 204 (26.6)**	**<.001**
Dementia	18	**699 (59.1)**	**653 (14.4)**	**<.001**
Diabetes mellitus	18	323 (27.3)	1 175 (25.9)	.338
Chronic pulmonary disease‡	29	**168 (14.2)**	**929 (20.5)**	**<.001**
Malignancy§	25	**124 (10.5)**	**625 (13.8)**	**.003**
Chronic kidney disease‖	18	112 (9.5)	474 (10.5)	.317
Symptoms				
Dyspnea	31	**762 (64.6)**	**2 644 (58.5)**	**<.001**
Cough	30	**493 (41.9)**	**3 167 (70.0)**	**<.001**
Fatigue	94	**322 (27.8)**	**1 907 (42.6)**	**<.001**
Anorexia	101	**216 (18.5)**	**992 (22.2)**	**.007**
Diarrhea	65	**134 (11.5)**	**870 (19.3)**	**<.001**
Vomiting	72	66 (5.7)	313 (7.0)	.115
Duration of symptoms in days, median (IQR)	75	**3.0 (1.0–6.0)**	**6.0 (3.0–8.0)**	**<.001**
Physical examination				
Oxygen saturation<94%	155	**575 (50.0)**	**2 361 (53.3)**	**.045**
Temperature ≥37.8°C	194	**224 (19.7)**	**975 (22.1)**	**.077**
Hypotension	212	**118 (10.6)**	**262 (5.9)**	**<.001**
Tachycardia	165	**251 (22.1)**	**867 (19.6)**	**.062**
Tachypnea	132	**555 (48.1)**	**2 700 (60.7)**	**<.001**
Confusion	50	**519 (44.1)**	**872 (19.3)**	**<.001**
Pulmonary rales	130	**523 (44.8)**	**1 670 (37.7)**	**<.0001**
qSOFA index ≥2	0	**324 (27.3)**	**537 (11.9)**	**<.001**
Chest x-ray findings	0			**<.001**
Normal		**303 (27.1)**	**581 (12.9)**	
Unilateral infiltrates		**232 (20.7)**	**835 (18.5)**	
Bilateral infiltrates		**584 (52.2)**	**3 092 (68.6)**	
Laboratory findings				
Complete blood count				
Leukocytes (×10³/μL)	69	**7.54 (5.50–10.43)**	**6.57 (4.99–8.87)**	**<.001**
Neutrophils (×10³/μL)	92	**5.57 (3.80–8.50)**	**4.90 (3.40–7.20)**	**<.001**
Lymphocytes (×10³/μL)	92	**0.96 (0.63–1.40)**	**0.84 (0.60–1.20)**	**<.001**
Hemoglobin (g/dL)	65	**12.7 (11.5–14.1)**	**13.3 (12.1–14.5)**	**<.001**
Platelet count (×10³/μL)	65	**193 (149–258)**	**178 (138–233)**	**<.001**
Arterial blood gases				
pH	2549	7.44 (7.40–7.48)	7.44 (7.41–7.47)	.101
PO_2 (mmHg)	2539	65 (54–78.9)	64 (54–75.1)	.0124
PO_2/FiO_2 ratio	2786	**261 (200–322)**	**279 (219–323)**	**.010**
Serum biochemistry				
Glucose (mg/dL)	232	**125 (103–159)**	**119 (103–149)**	.003
eGFR (<45 ml/min/1.73 m²)	81	**51.0 (33.8–72.5)**	**59.4 (41.1–78.6)**	**<.001**
Lactate dehydrogenase (U/L)	953	**318 (235–452)**	**338 (157–465)**	**<.001**
AST (U/L)	1339	**29 (20–43)**	**35 (25–51)**	**<.001**
ALT (U/L)	511	**19 (13–31)**	**25 (16–37)**	**<.001**
C-reactive protein (mg/L)	250	65.9 (20.8–140.1)	73.0 (24.0–144)	.057
Venous lactate (mmol/L)	3087	1.7(1.1–2.4)	6 (1.2–2.7)	.071
Procalcitonin (ng/mL)	2972	0.13 (0.08–0.31)	0.13 (0.70–0.30)	.375
Interleukin-6 (pg/mL)	5167	37.5 (15.1–19.7)	36.6 (15.5–71.4)	.901

Table 1. Conitnued

	Missing values	LTCF (n = 1 185)	Community-dwelling (n = 4 548)	p value
D-dimer (ng/mL)	1377	**1 211 (677–2 445)**	**874 (468–1 737)**	**<.001**
Serum ferritin (µg/L)	3522	**412 (187–8 429)**	**523 (151–1 130)**	**<.001**

Notes: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CCI = Charlson Comorbidity Index; eGFR = estimated glomerular filtration rate; FiO_2 = fraction of inspired oxygen; IQR = interquartile range; LTCF = long-term care facility; *N* (%) = number of cases (percentage); qSOFA = quick sequential organ failure assessment.

*Non-atherosclerotic heart disease includes atrial fibrillation and/or heart failure. †Atherosclerotic cardiovascular disease includes coronary, cerebrovascular, and/or peripheral vascular disease. ‡Chronic pulmonary disease includes chronic obstructive pulmonary diseases and/or asthma. §Malignancy includes solid tumors or hematological neoplasia. ‖Chronic kidney disease is defined as an estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2 according to the CKD-EPI equation. Statistically significant differences are indicated in bold.

Table 2. Treatment, Complications, and Outcomes in Patients ≥ 75 y of Age Hospitalized with COVID-19 Living in LTCF

Treatment	Missing values	LTCF (n = 1 185)	Community-dwelling (n = 4 548)	p Value
Immunomodulatory therapy				
Systemic corticosteroids	41	**420 (35.6)**	**1 826 (40.5)**	**.002**
Tocilizumab	38	**20 (1.7)**	**280 (6.2)**	**<.001**
Colchicine	87	21 (1.8)	54 (1.2)	.127
Anakinra	74	**0**	**27 (0.6)**	**.008**
Baricitinib	953	7 (0.6)	21 (0.6)	.0901
Immunoglobulin	92	2 (0.2)	14 (0.39	.410
Ventilatory therapy				
High-flow nasal cannula oxygen	62	**57 (4.8)**	**379 (8.4)**	**<.001**
Noninvasive mechanical ventilation	43	**16 (1.4)**	**227 (6.1)**	**<.001**
Invasive mechanic ventilation	39	**7 (0.6)**	**158 (3.5)**	**<.001**
Anticoagulant therapy				
Oral anticoagulants	45	78 (6.6)	289 (6.4)	.804
Low-molecular-weight heparin	42	**927 (78.5)**	**3 771 (83.6)**	**<.001**
Complications				
ARDS, severe	36	**235 (20.0)**	**1 221 (27.0)**	**<.001**
Acute kidney failure	36	**302 (25.6)**	**959 (21.2)**	**.001**
Pneumonia	23	**215 (18.3)**	**581 (12.8)**	**<.001**
Acute heart failure	20	119 (10.1)	468 (10.3)	.792
Sepsis	21	109 (9.2)	343 (7.6)	.060
Multiple organ dysfunction syndrome	30	106 (9.0)	430 (9.5)	.593
Arrhythmia	30	73 (6.29	265 (5.9)	.678
Shock	28	46 (3.9)	224 (5.09	.130
Venous thromboembolism	32	25 (2.1)	89 (2.0)	.740
Acute coronary syndrome	21	16 (1.4)	56 (1.2)	.744
Epileptic seizures	17	13 (1.19	29 (0.6)	.099
Acute peripheral ischemic	28	**12 (1.0)**	**20 (0.4)**	**.019**
Myocarditis	21	10 (0.8)	39 (0.9)	.985
Intravascular coagulation	31	**7 (0.6)**	**62 (1.4)**	**.030**
Stroke	21	6 (0.5)	42 (0.9)	.651
Outcomes				
Intensive care unit admission	4	**9 (0.8)**	**201 (4.4)**	**<.001**
Readmission	194	60 (5.2)	213 (4.9)	.608
Death	45	**505 (43.3)**	**1794 (39.7)**	**.026**
Days of hospitalization, median (IQR)	75	**13 (7–20)**	**15 (11–22)**	**<.001**

Notes: ARDS = acute respiratory distress syndrome; IQR = interquartile range; LTCF = long-term care facilities; *N* (%) = number of cases (percentage). Statistically significant differences are indicated in bold.

mechanical ventilation, and invasive mechanic ventilation) and fewer were admitted to the intensive care unit (0.8% vs 4.4%; $p < .001$), though in-hospital mortality was higher in this group than among community-dwelling older adults (43.3% vs 39.7%; $p = .026$). LTCF residents had shorter hospital stays than community-dwelling older adults (median stay of 13 vs 15 days; $p < .001$; Table 2).

After adjusting for sex, age, functional dependence, and comorbidities (hypertension, dyslipidemia, non-atherosclerotic heart diseases, atherosclerotic cardiovascular diseases, dementia, diabetes mellitus, chronic pulmonary disease, malignancy, and moderate-severe renal disease), severe ARDS (aOR: 0.71, 95% CI: 0.61–0.86), noninvasive mechanical ventilation (aOR: 0.53, 95% CI: 0.030–0.95), and mortality (aOR: 0.74, 95% CI: 0.62–0.87)

Table 3. Treatment, Complications, and Outcomes in Patients ≥ 75 y of Age Hospitalized with COVID-19 Living in LTCF Compared to Community-dwelling Older Adults. Multivariable Logistic Regression Analyses

	Crude OR (95% CIs)	Adjusted OR* (95% CIs)	*p* Value
Immunomodulatory therapy			
Systemic corticosteroids	0.81 (0.71–0.92)	0.97 (0.82–1.15)	.779
Tocilizumab	0.26 (0.16–0.41)	1–06 (0.67–1.82)	.829
Ventilatory therapy			
High-flow nasal cannula oxygen	0.53 (0.41–0.73)	0.87 (0.62–1.24)	.427
Noninvasive mechanical ventilation	0.21 (0.12–0.35)	**0.53 (0.30–0.95)**	**.035**
Invasive mechanic ventilation	0.16 (0.07–0.35)	1.44 (0.61–3.43)	.399
Anticoagulant therapy			
Low-molecular-weight heparin	0.71 (0.61–0.83)	0.73 (068–1.01)	.073
Complications			
ARDS, severe	0.67 (0.58–0.79)	**0.71 (0.61–0.86)**	**<.001**
Acute kidney failure	1.28 (1.10–1.48)	1.16 (0.96–1.40)	.126
Pneumonia	1.51 (1.27–1.80)	**1.29 (1.05–1.61)**	**.018**
Intravascular coagulation	0.43 (0.19–0.94)	0.51 (0.21–1.23)	.135
Acute peripheral ischemia	2.30 (1.12–4.73)	1.87 (0.76–4.59)	.168
Outcome			
Intensive care unit admission	0.18 (0.08–0.32)	1.63 (0.61–2.94)	.460
Readmission	1.08 (0.80–1.45)	0.82 (0.62–1.26)	.522
Death	1.16 (1.01–1.32)	**0.74 (0.62–0.87)**	**<.001**

Notes: *Adjusted by sex, age, functional dependence, and comorbidities (hypertension, dyslipidemia, non-atherosclerotic heart diseases, atherosclerotic cardiovascular diseases, dementia, diabetes mellitus, chronic pulmonary disease, malignancy, chronic kidney disease).

ARDS = acute respiratory distress syndrome; LTCF = long-term care facilities. Statistically significant differences are indicated in bold.

were less frequent among LTCF residents than community-dwelling older adults, but pneumonia was more frequent (aOR: 1.29, 95% CI: 1.05–1.61; Table 3).

Risk Factors at Admission Associated with In-Hospital Mortality in LTCF Residents

Data on IHM were missing for 18 of the 1 185 LTCF residents included in this work. The IHM rate among LTCF changes was 46.9% (662 deaths out of 1 167 patients analyzed) (Supplementary Figure 1).

The baseline clinical characteristics, clinical presentation, and laboratory data at admission along with in-hospital treatment and complications in LTCF residents hospitalized due to COVID-19 grouped as non-survivors versus survivors are shown in Supplementary Tables 1 and 2.

On the multivariable analysis, the clinical conditions and laboratory findings at admission associated with IHM in LTCF residents were severe functional dependence (aOR: 1.79; 95% CI: 1.13–2.83; p = .012), dyspnea (aOR: 1.66; 95% CI: 1.16–2.39; p = .004), oxygen saturation <94% (aOR: 1.73; 95% CI: 1.27–2.37; p = .001), temperature ≥37.8°C (aOR: 1.62; 95% CI: 1.11–2.38; p = .013); qSOFA index ≥2 (aOR: 1.62; 95% CI: 1.11–2.38; p = .013), bilateral infiltrates (aOR: 1.98; 95% CI: 1.24–2.98; p < .001), and high C-reactive protein levels (aOR: 1.005; 95% CI: 1.003–1.007; p < .001). In this model, the p value for the Hosmer–Lemeshow goodness of fit test was 0.211, with an AUC of 0.856 (95% CI: 0.832–0.887), which indicates good predictive ability (Table 4).

Lastly, on the multivariable analysis, in-hospital complications found to be associated with IHM were severe ARDS (aOR: 97.86; 95% CI: 46.5–205; p < .001), multiple organ dysfunction syndrome (aOR: 36.66; 95% CI: 8.18–164; p < .001), moderate ARDS (aOR: 9.04; 95% CI: 5.40–15.12; p < .001), sepsis (aOR: 4.12; 95% CI: 2.07–8.19; p < .001), and acute kidney failure (aOR: 2.35; 95% CI: 1.58–3.40; p < .001). In this model, the p value for the Hosmer–Lemeshow goodness of fit test was 0.456, with an AUC of 0.881 (95% CI: 0.859–0.903), which indicates good predictive ability (Table 5).

Discussion

The COVID-19 pandemic has taken a huge toll on older adults (4,16–18) and severely impacted those living in LTCF (13,19–21). Therefore, this study focuses on analyzing the profile and risk factors for IHM of LTCF residents hospitalized with COVID-19 as compared to community-dwelling older adults. As was expected, the LTCF residents in our study were older, mainly female, and had a higher degree of functional dependence and number of comorbidities than community-dwelling older adults (4,6,19–21). The higher percentage of female versus male LTCF patients observed in our series may be explained by the fact that more than 70% of LTCF residents in Spain are women (22).

In our study, LTCF residents represent 20% of those ≥ 75 years hospitalized with COVID-19. LTCF residents were less symptomatic at admission than community-dwelling older adults, though dyspnea and confusion were more frequent. It is well known that confusion is a very common clinical presentation in older patients with critical illness, especially in individuals with pre-existing cognitive impairment (23,24). In older patients with COVID-19, hypoactive delirium has been reported as a very common symptom both among LTCF residents and patients with dementia (13,23–25).

Interestingly, patients living in LTCF had RT-PCR tests performed earlier and a shorter duration of symptoms before admission compared to community-dwelling older adults, despite the fact they were less symptomatic. This finding suggests that these older adults were more closely monitored by professional LTCF staff, which would have allowed for early detection of geriatric syndromes triggered by COVID-19 and led to prompt transfer to

Table 4. Risk of Mortality According to Clinical, Radiological, and Analytic Findings at Admission in Patients ≥ 75 y of Age Hospitalized with COVID-19 Living in LTCF (bivariable and multivariable analysis)

	Crude OR (95% CI)	Adjusted OR (95% CI)	*p* Value
Age	1.00 (0.98–1.02)	0.99 (0.97–1.02)	.961
Sex, Male	1.19 (1.08–1.36)	1.16 (0.84–1.60)	.340
Degree of functional dependence			
Independent or mild	1	1	
Moderate	1.29 (0.90–1.84)	1.13 (0.71–1.82)	.580
Severe	1.99 (1.41–2.79)	**1.79 (1.13–2.83)**	**.012**
Comorbidities			
CCI	1.14 (1.07–1.21)	NI	
Non-atherosclerotic heart disease*	1.35 (1.06–1.76)	1.35 (0.92–1.88)	.069
Atherosclerotic cardiovascular disease†	1.37 (1.07–1.76)	1.20 (0.86–1.76)	.270
Chronic kidney disease‡	1.89 (1.27–2.81)	1.18 (0.67–2.05)	.552
Dementia	1.38 (1.01–1.63)	0.81 (0.56–1.16)	.267
Symptoms			
Shortness of breath	3.27 (2.51–4.26)	**1.66 (1.16–2.39)**	**.004**
Diarrhea	0.65 (0.44–0.95)	0.74 (0.432–1.26)	.270
Anorexia		1.46 (0.97–2.20)	.065
Physical examination			
Oxygen saturation<94%	3.04 (2.38–3.88)	**1.73 (1.27–2.37)**	**.001**
Temperature ≥37.8°C	1.77 (1.31–2.38)	**1.62 (1.11–2.38)**	**.013**
Hypotension	2.36 (1.58–3.51)	NI	
Tachycardia	2.45 (1.82–3.27)	1.094 (0.74–1.60)	.621
Tachypnea	4.47 (3.48–5.74)	NI	
Confusion	2.45 (1.93–3.11)	NI	
Pulmonary rales	1.64 (1.29–2.07)	1.04 (0.76–1.43)	.776
qSOFA index ≥2	3.85 (3.01–5.21)	**2.39 (1.69–3.38)**	**<.001**
Chest x-ray			
Normal	1	1	
Unilateral infiltrates	1.64 (1.14–2.37)	1.27 (0.80–2.02)	.292
Bilateral infiltrates	2.95 (2.18–3.98)	**1.98 (1.24–2.92)**	**<.001**
Laboratory findings			
Complete blood count			
Leukocytes $\times 10^3/\mu L$	1.000 (1.000–1.0)	1.000 (1.000–1.000)	.852
Neutrophils $\times 10^3/\mu L$	1.000 (1.000–1.0)	1.000 (1.000–1.000)	.128
Lymphocytes $\times 10^3/\mu L$	1.000 (1.000–1.0)	1.000 (1.000–1.000)	.172
Arterial blood gases			
pH	0.008 (0.001–0.09)	NI	
PO2 mmHg	0.98 (0.98–0.99)	NI	
PO2/FiO2 ratio ≤200	0.991 (0.988–0.993)	NI	
Biochemistry			
Glucose (mg/dL)	1.003 (1.002–1.005)	1.00 (0.999–1.002)	.666
eGFR (<45 mL/min/1.73 m^2)	0.984 (0.978–0.989)	**0.993 (0.986–1.000)**	**.044**
Lactate dehydrogenase (U/L)	1.004 (1.003–1.005)		
AST (U/L)	1.010 (1.005–1.014)	NI	
ALT (U/L)	1.004 (1.001–1.007)	NI	
C-reactive protein (mg/L)	1.008 (1.007–1.010)	**1.005 (1.003–1.007)**	**<.001**
Venous lactate (mmol/L)	1.038 (0.995–1.089)	NI	
Procalcitonin (ng/mL)	1.445 (1.187–1.781)	NI	
Interleukin-6 (pg/mL)	1.014 (1.004–1.024)	NI	
D-dimer (ng/mL)	1.000 (1.000–1.000)	NI	
Serum ferritin (μg/L)	1.000 (1.000–1.000)	NI	

Notes: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CCI = Charlson Comorbidity Index; CI = confidence interval; eGFR = estimated glomerular filtration rate; LTCF = long-term care facilities; NI = not included in the multivariable analysis; OR = odds ratio; qSOFA = quick sequential organ failure assessment.

*Non-atherosclerotic heart disease includes atrial fibrillation or/and heart failure. †Atherosclerotic cardiovascular disease includes coronary, cerebrovascular, and/or peripheral vascular disease. ‡Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73 m^2 according to the CKD-EPI equation.

Statistically significant differences are indicated in bold.

the emergency department. In Spain, LTCF residents who tested positive for COVID-19 were transferred to the hospital according to the attending physician's discretion, clinical judgment, and local protocols. These protocols varied across the different regions of Spain and changed throughout the pandemic based on the availably of hospital resources and the feasibility of establishing

Table 5. Risk of Mortality According to Complications in Patients > 75 y Old Hospitalized with COVID-19 Living in LTCF (bivariable and multivariable analysis)

	Crude OR (95% CI)	Adjusted OR (95% CI)*	*p* value
Complications			
ARDS, Mild	1.20 (0.68–2.12)	1.00 (0.51–1.92)	.922
ARDS, Moderate	9.81 (6.18–15.57)	**9.04 (5.40–15.12)**	**<.001**
ARDS, Severe	84.14 (42.3–167)	**97.86 (46.5–205)**	**<.001**
Acute kidney failure	2.91 (2.24–3.83)	**2.35 (1.58–3.40)**	**<.001**
Pneumonia	2.09 (1.54–2.84)	1.31 (.84–205)	.222
Acute heart failure	1.98 (1.34–2.95)	0.77 (.42–1.42)	.411
Sepsis	7.78 (4.62–13.1)	**4.12 (2.07–8.19)**	**<.001**
Multiple organ dysfunction syndrome	85.75 (21.0–349)	**36.66 (8.18–164)**	**<.001**
Shock	64.9 (8.9–4739	9.00 (.95–84.77)	.055
Venous thromboembolism	0.28 (0.09–0.84)	**0.09 (0.01–0.54)**	**.008**
Acute coronary syndrome	4.01 (1.28–12.5)	**4.14 (0.98–17.5)**	**.042**

Notes: ARDS = acute respiratory distress syndrome; LTCF = long-term care facilities
*Adjusted by age, sex, and other complications.
Statistically significant differences are indicated in bold.

isolation areas within LTCF for residents with known or suspected COVID-19 (10).

LTCF residents represent 20% of the total number of COVID-19 deaths among the population ≥75 years. Although LTCF residents had higher IHM, after adjusting for age, sex, and comorbidities, their mortality risk was in fact significantly lower than that of community-dwelling older adults. This low risk of IHM was in spite of the fact that a number of therapies that have been proven effective against COVID-19 (corticosteroids, low-molecular-weight heparin, high-flow oxygen, and noninvasive mechanical ventilation) were used less frequently in LTCF residents. Thus, the early hospital admission of LTCF residents could explain their lower mortality risk compared to community-dwelling older adults. This earlier recognition of symptoms and prompt treatment of COVID-19 have also been proposed as factors underlying the lower mortality risk observed specifically in the Spanish LTCF that were medicalized during the first wave of infections (10,23). These measures were part of a nationwide plan to address COVID-19 outbreaks in these facilities and allowed residents to be treated within the facility (23).

The factors associated with poor outcomes among LTCF residents in this study were generally similar to those described in other cohorts of older adults hospitalized with COVID-19 (13,20,21). However, in our population of patients from LTCF, male sex was not associated with a worse prognosis. This is in contrast with other reports on the general population (26) and on very old patients with COVID-19 (4,26).

Although comorbidities are very common in older patients with COVID-19 (27,28), we did not find a correlation between age-adjusted CCI and mortality among LTCF residents in our series. This finding has indeed been previously reported in other studies performed in very old patients hospitalized with COVID-19 as well as in series on medicalized nursing homes with COVID-19 outbreaks (3,4,24). Unlike comorbidity burden, functional status is associated with prognosis in older adults with COVID-19. As has been described in older adults hospitalized due to COVID-19 (3,4), we confirmed that a severe degree of functional dependence prior to admission (defined as a Barthel Index ≤60) was an independent predictor of death in LTCF residents.

Along these lines, our study confirms the utility of qSOFA (a quick point-of-care score based on respiratory rate, systolic blood pressure, and mental status) (29) in identifying patients with COVID-19 who are at greater risk of poor outcomes (30,31). In view of our results in LTCF residents and prior reports on very old patients (4), we strongly recommend administering the qSOFA upon admission in older adults with COVID-19.

Just as with other diseases, we found that COVID-19 IHM risk depends on 2 major factors: the severity of the disease itself (as observed in this study through clinical and biological parameters) and the patient's baseline status (as observed this study through patients' functional status) (3).

Finally, we also observed that acute kidney injury, a common complication in hospitalized adults, is associated with higher mortality in LTCF residents, a finding recently described in patients ≥65 years of age with COVID-19 (32). Moreover, as has been described in the general population (1,33,34) and in older adults (4,16–18,34), both ARDS and multiple organ dysfunction syndrome are potent predictors of mortality in LTCF patients hospitalized with COVID-19.

Among the strengths of our study are the large number of patients analyzed and its multicenter, nationwide design. However, we recognize some limitations. First, its observational design does not allow us to determine causal relationships. Second, our study was conducted in LTCF residents hospitalized with severe SARS-CoV-2 infection, thus our conclusions cannot be extrapolated to non-hospitalized LTCF residents with COVID-19. Third, we did not have data on frailty and some geriatric syndromes (falls, delirium, malnutrition, etc.). Finally, an important limitation in the study's design is the potential selection bias of including LTCF residents in the study population. Decisions regarding the transfer of residents from LTCF to hospitals may have been influenced by expectations regarding the life expectancy of these LTCF residents and/or their families' decisions regarding more aggressive therapies. It is possible that the most fragile LTCF residents and/or those with most severe COVID-19 may have remained in LTCF for appropriate palliative care. This may explain the lack of association found in our study between male sex and older age, which have been described as factors of worse prognosis in COVID-19. Furthermore, the lower risk of ICU admission in LTCF patients may be a result of their underlying conditions, such as frailty, comorbidities, or older age, which in turn may have been factors in them not receiving assisted ventilation or other intensive therapies (e.g., corticosteroids, heparin, tocilizumab).

In conclusion, we found that LTCF residents hospitalized due to COVID-19 had a different clinical profile than community-dwelling older adults (fewer classic COVID-19 symptoms, shorter duration of symptoms, and higher frequency of confusion). This study also provides further evidence on the usefulness of measuring baseline functional status and the qSOFA score for estimating the prognosis of LTCF residents with COVID-19. Finally, it is important to highlight that residing in a LTCF per se was not associated with poor prognosis. Although the risk of mortality was higher among LTCF residents than community-dwelling older adults hospitalized with COVID-19, after adjusting the analysis for the confounding effect of underlying conditions associated with a higher risk of mortality—which are more prevalent among LTCF residents—LTCF patients were found to have better outcomes than community-dwelling older adults (4,18,26–28,33). Our findings highlight the importance of routinely performing a comprehensive geriatric assessment in older adults who live in LTCF and who have COVID-19, as their baseline functional status is more important for guiding the decision-making process than their comorbidities.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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List of the SEMI-COVID-19 Network members is given in the Supplementary Appendix.

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Conflict of Interest

None declared.

Author Contributions

J-M.R.-R., M.B.-W., and R.G.-H. designed the study, had full access to all data in the study, and takes responsibility for the integrity and accuracy of the data analysis. I.F.-M., A.L.-S, C.L.-R., M.-M.G.-A., J-J.M.-S., C.J.-J., M.M.-S, P.L.-Q., M.R.-R., D.P.-R., C.G.-S.-N-, R.G.-V., P.S.-E., A.H.-M., and A.G.-N. contributed to data acquisition and data interpretation. J.-M.R.-R., and R.G.-H. were responsible for literature search, manuscript writing, and data analysis. J.-M.R.-R., M.B.-W., I.F.-M., and R.G.-H. were responsible for supervision of data collection and data management. All authors reviewed and approved the final version of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. J.-M.R.-R., and R.G.-H. are the guarantor.

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