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ORIGINAL ARTICLE

Factors associated with mortality due to SARS-CoV-2 in the population over 75 years of age in the Community of Madrid☆

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Abstract
Objective: Various studies have identified factors associated with risk of mortality in patients with SARS-CoV-2 infection. However, their sample size has often been limited and their results partially contradictory. This study evaluated factors associated with COVID-19 mortality in the population of Madrid over 75 years of age, in infected patients, and in hospitalized patients up to January 2021.
Patients and Methods: This population-based cohort study analyzed all residents of the Community of Madrid born before January 1, 1945 who were alive as of December 31, 2019. Demographic and clinical data were obtained from primary care electronic medical records (PC-Madrid), data on hospital admissions from the *Conjunto Mínimo Básico de Datos* (CMBD, Minimum Data Set), and data on mortality from the *Índice Nacional de Defunciones* (INDEF, National Death Index). Data on SARS-CoV-2 infection, hospitalization, and death were collected from March 1, 2020 to January 31, 2021.

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Results: A total of 587,603 subjects were included in the cohort. Of them, 41,603 (7.1%) had confirmed SARS-CoV-2 infection, of which 22,362 (53.7% of the infected individuals) were hospitalized and 11,251 (27%) died. Male sex and age were the factors most closely associated with mortality, though many comorbidities also had an influence. The associations were stronger in the analysis of the total population than in the analysis of infected or hospitalized patients. Mortality among hospitalized patients was lower during the second wave (33.4%) than during the first wave (41.2%) of the pandemic.
Conclusion: Age, sex, and numerous comorbidities are associated with risk of death due to COVID-19. Mortality in hospitalized patients declined notably after the first wave of the pandemic.

PALABRAS CLAVE
COVID-19;
SARS-CoV-2;
Ancianos;
Factores de riesgo;
Mortalidad

Factores asociados con la mortalidad por SARS-CoV-2 en la población mayor de 75 años de la Comunidad de Madrid

Resumen
Objetivo: Diversos estudios han identificado factores asociados con el riesgo de muerte en pacientes infectados por SARS-CoV-2. Sin embargo, su tamaño muestral ha sido muchas veces limitado, y sus resultados parcialmente contradictorios. Este estudio ha evaluado los factores asociados con la mortalidad por COVID-19 en la población madrileña mayor de 75 años, en los pacientes infectados y en los hospitalizados hasta enero de 2021.
Pacientes y métodos: Estudio de cohortes de base poblacional con todos los residentes de la Comunidad de Madrid nacidos antes del 1 de enero de 1945 y vivos a 31 de diciembre de 2019. Se obtuvieron variables demográficas y clínicas de la historia clínica electrónica de atención primaria (AP-Madrid), de los ingresos hospitalarios a través del Conjunto Mínimo Básico de Datos (CMBD) y de la mortalidad a través del Índice Nacional de Defunciones (INDEF). Se recogieron los datos de infección, hospitalización y muerte por SARS-CoV-2 entre el 1 de marzo de 2020 y el 31 de enero de 2021.
Resultados: De los 587.603 sujetos incluidos en la cohorte, 41.603 (7,1%) desarrollaron una infección confirmada por SARS-CoV-2. De ellos, 22.362 (53,7% de los infectados) se hospitalizaron y 11.251 (27%) murieron. El sexo masculino y la edad fueron los factores más asociados con la mortalidad, si bien también contribuyeron numerosas comorbilidades. La asociación fue de mayor magnitud en los análisis poblacionales que en los análisis con pacientes infectados u hospitalizados. La mortalidad en los hospitalizados fue menor en la segunda ola (33,4%) que en la primera ola (41,2%) de la pandemia.
Conclusión: La edad, el sexo y las numerosas comorbilidades se asocian con el riesgo de muerte por COVID-19. La mortalidad en los pacientes hospitalizados se redujo apreciablemente después de la primera ola de la pandemia.

Introduction

The risk of SARS-CoV-2 infection and its clinical progress are not very predictable and the factors which trigger greater susceptibility to contagion and worse disease progression are not fully known.

The percentage of patients with severe disease who require hospital admission and/or who die is very high. The factors which have systemically been associated with worse disease progress are male sex and old age.[1–3]

In Spain, the mortality rate in infected individuals older than 80 years is 4.6% and 11.6% in women and men, respectively, for those with a confirmed COVID-19 diagnosis. The rate increases to 6.5% and 16.4% if the calculation is based on excess mortality.[4] In individuals older than 75 years who required hospitalization, the case fatality rate reached 36%.[5]

In addition to age and sex, various factors have been related to worse disease progress.[2,3,6,7] However, these factors are occasionally contradictory;[8,9] they may differ in older adults, the population segment which has the highest mortality, and could be influenced by the type of population studied.

The identification of population segments with a worse prognosis is important for establishing measures for early diagnosis, for suggesting preventive

strategies, and for starting early preventive treatments.

Since 2015, data have been collected on a cohort of all residents in the Community of Madrid (CM) born before January 1, 1945. Their demographic, clinical, and anthropometric data have been gathered at baseline and during follow-up. This cohort allowed for evaluating factors associated with SARS-CoV-2 mortality in the total Madrid population older than 75 years, in the infected patients, and in the hospitalized patients.

Methods

Study design

The study participants came from a cohort started on January 1, 2015 to evaluate factors associated with the development of cardiovascular disease in older adults. This cohort included all residents in the CM born before January 1, 1945. The CM provides healthcare to 100% of the population through 3,881 primary care physicians who work at 424 health centers. All residents have a primary care electronic medical record (PC-Madrid).

As of December 31, 2019, 587,603 participants were alive and had at least one entry in their electronic medical record during the previous two years (active); they are the study population.

From the end of February 2020 to January 31, 2021, data on infection, hospitalization, or death due to SARS-CoV-2 were collected. Cases of infection in the first wave were all those which occurred before July 1, 2020 and cases in the second wave were all those which occurred after that date.

The study was approved by the Clinical Research Ethics Committee of the Ramón y Cajal University Hospital of Madrid.

Variables and definitions

The data collected on the AP-Madrid medical record were age, sex, cardiovascular risk factors (hypertension, diabetes mellitus, presence of kidney failure, tobacco use, and body mass index), and diseases present as of December 31, 2019.

Blood tests and anthropometric measurements taken between January 1, 2015—the cohort's start date—and December 31, 2019 were gathered. The last value included on the record was used for the analysis.

The Spanish Society of Epidemiology's Deprivation Index (DI2011), a measurement of the degree of economic deprivation of the population residing in each enumeration district, was obtained from the General Directorate of Public Health. This index combines information on six socioeconomic indicators: percentage of the population who are manual laborers, percentage of the population who are temporary workers, percentage of the population who are unemployed, percentage of the population with insufficient education, percentage of the young population with insufficient education, and percentage of primary residences without access to the internet. The data come from the 2011 census and serve to estimate social inequalities in health and healthcare.[10]

SARS-CoV-2 infection was considered confirmed when there was a positive RT-PCR or antigen test.

Hospitalization due to COVID-19 was defined as any hospitalization in which SARS-CoV-2 infection was recorded on the medical record or any hospitalization which occurred in the 15 days after a confirmed SARS-CoV-2 infection diagnosis. In the case of more than one admission with said diagnosis, only the first was considered. Admissions were obtained from the Minimum Basic Data Set upon hospital discharge, a set of clinical information recorded in patients' electronic medical records, provided by the CM Regional Ministry of Health for public hospitals only.

SARS-CoV-2 infection was considered the cause of death when it was reflected as such on the medical record or when the death, determined according to the death index (INDEF, for its initials in Spanish), occurred in the 15 days after a confirmed virus infection.

All records were anonymized at the time of their inclusion in the database. The validity of the primary care electronic medical record for research studies has previously been demonstrated[11] and this database has been used for various epidemiological studies.[12,13]

Statistical analysis

Continuous variables are shown as mean ± standard deviation and categorical variables are shown as percentages. Comparisons among continuous variables were made using Student's t test and among categorical variables using the χ^2 test. The PI2011 for the entire Madrid population was classified into quartiles for its use. To evaluate factors associated with mortality, a logistic regression analysis was conducted in three groups of participants:

1 A multinomial logistic regression analysis for the entire population included in the cohort (587,603 participants) which considered competing mortality, analyzing mortality as the dependent variable in three categories: the 11,251 subjects who died due to COVID-19, the 36,283 who died due to causes not unequivocally attributable to COVID-19, and those alive at the end of follow-up. The last category was the reference category.
2 A binary logistic regression analysis in patients with a confirmed diagnosis of SARS-CoV-2 infection (41,603 patients).
3 A binary logistic regression analysis in patients hospitalized with a diagnosis of SARS-CoV-2 infection (22,362 patients).

The same analyses were conducted separately for the first disease wave (until July 1, 2020) and for subsequent waves (from that date until January 31, 2021).

Factors which had a *p* value less than 0.10 on the univariate analysis were selected for the multivariate analysis as well as those for which, in light of theoretical or empirical knowledge, were considered to be related to the dependent variable. The validity of the model was evaluated by estimating its goodness of fit using the χ^2 test or the Hosmer–Lemeshow test.

Other exploratory regression models that included body mass index and markers of overall clinical condition, such as

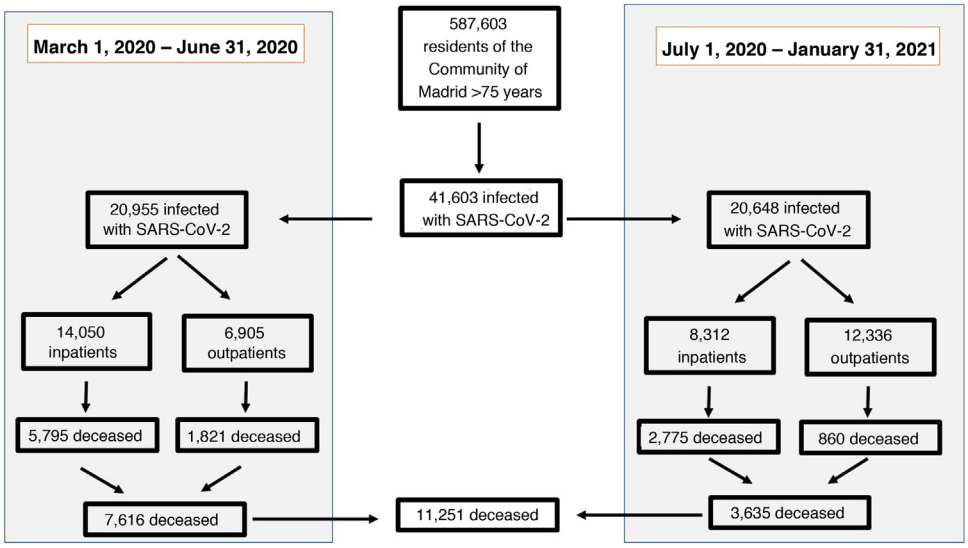

Figure 1 Flowchart of patients older than 75 years from the Community of Madrid who were infected, hospitalized, or died due to SARS-CoV-2 during the first and subsequent waves.

plasma albumin concentration, were also calculated. Given that not all patients had weight or height measurements or blood test results in the last five years, the sample sizes in these analyses were smaller. The study's associations were summarized as odds ratios (OR) with their respective 95% confidence intervals (CI).

The data analysis was performed with SPSS for Windows, v. 19.0; IBM Corp, Armonk, New York, USA.

Results

Of the 587,603 residents in the CM born before January 1, 1945 who were alive and active as of December 31, 2019, 41,603 (7.1%) had a confirmed SARS-CoV-2 infection: 20,955 during the first wave and 20,648 between July 1, 2020 and January 31, 2021. The temporal distribution of confirmed infections can be seen in Appendix A Fig. 1 of the additional material. A total of 53.7% of those infected (22,362 patients) were hospitalized. In total, 11,251 died as a consequence of infection: 1.9% of the total study population, 27% of the total number of infected individuals, and 38.2% of the total number of hospitalized individuals (Fig. 1).

The demographic and clinical data on the total population, on the infected patients, and on the hospitalized patients can be seen in Table 1. In regard to the general population, age, the percentage of men, and the prevalence of cardiovascular risk factors and comorbidities were higher in the group of infected patients and even higher in hospitalized subjects. One exception was patients with Alzheimer's disease, in whom the percentage of hospitalized individuals was lower than the percentage of infected individuals. Subjects with a lower deprivation index, which represented a higher percentage of the total study population, constituted a smaller percentage of infected patients and even smaller percentage of hospitalized patients.

The differential characteristics of those who died in each of the three groups (total population, infected population, and hospitalized population) can be seen in Table 2. Mortality increased with age and was greater among men and, in general, in those with most comorbidities (Table 2). Mortality was 20.2% in subjects 85 years of age or younger and 33.1% in those older than 85 years.

On the multivariate analysis (Fig. 2 and Appendix A Table 1 of the additional material), when the total population was analyzed, it was verified that age, male sex, and all comorbidities were associated with greater mortality. Compared to those with less socioeconomic deprivation, those with average deprivation levels had a higher mortality rate. In general, the intensity of most comorbidity's association with mortality decreased from the total population to infected subjects to hospitalized subjects. Some diseases even lost their association with mortality, such as in chronic liver disease, hypertension, rheumatoid arthritis, and chronic obstructive pulmonary disease (COPD).

The analyses were repeated with the forced entry of body mass index, yielding a significant result (OR: 1.011; 95%CI: 1.005–1.017 for each kg/m^2 unit) and without notable modifications in the remaining variables. Likewise, the inclusion of albumin was inversely associated with mortality (OR: 0.813; 95%CI: 0.759—0.870 for each mg/dL) without affecting the rest of the variables.

Of the 11,251 deceased individuals, 7,616 patients (1.3% of the total population, 36.3% of infected individuals) died during the first wave and 3,635 (0.6% of the total population, 17.6% of infected individuals) died during subsequent waves (until January 31, 2021). Though the characteristics of hospitalized patients did not notably differ during both periods (Appendix A Table 2 of the additional material), in-hospital mortality was greater in the first wave. During this wave, of the 14,050 hospitalized subjects, 5,795 (41.2%) died and during subsequent waves, of the 8,312 hospitalized subjects, 2,775 (33.4%) died.

Factors associated with mortality in the total population, mortality in infected subjects, and mortality in hospitalized subjects for the two periods analyzed separately can be seen in Fig. 3 and Appendix A Table 3 of the additional material. Though the trends were similar, in the second part of the

Table 1 Clinical characteristics of the population older than 75 years who are residents of the Community of Madrid, of infected patients, and of patients hospitalized due to SARS-CoV-2.

	Total population 587,603	Infected patients 41,603	Hospitalized patients 22,362
Age (years)	83.5 ± 5.8	84.7 ± 5.9	84.7 ± 5.8
Sex (% male)	38.3	42.4	48.8
Deprivation index (%)			
Less deprivation	28.4	25.8	22.5
Low-medium deprivation	23.2	25.1	24.9
Medium-high deprivation	25.1	24.8	26.3
High deprivation	23.2	24.3	26.3
Active cancer during the last 5 years (%)	5.2	5.8	6.5
Chronic liver disease (%)	1.0	1.1	1.3
Hypertension (%)	61.6	63.6	64.5
Diabetes (%)	23.7	27.8	30.0
Atrial fibrillation (%)	14.9	18.6	20.2
Prior thromboembolic disease (%)	3.8	5.0	5.5
Chronic renal failure (%)	6.0	7.5	8.6
Heart failure (%)	6.1	9.1	10.5
Chronic obstructive pulmonary disease or asthma (%)	10.4	13.2	15.4
Rheumatoid arthritis (%)	3.4	3.8	3.9
Alzheimer's disease (%)	8.0	13.7	12.7
Cardiovascular disease (%)			
Stroke (%)	5.9	8.1	8.5
Myocardial infarction (%)	4.5	5.7	6.6
Angina (%)	4.5	5.5	6.1
Peripheral arterial disease (%)	4.3	5.8	6.7
Excessive alcohol consumption (%)	1.1	1.4	1.6
Tobacco use (%)	4.9	4.8	5.4
Body mass index (kg/m^2)	28.0 ± 4.7	28.2 ± 4.8	28.4 ± 4.9

Table 2 Characteristics of patients who died due to COVID-19 compared to the total Madrid population, patients infected by SARS-CoV-2 who survived the infection, and patients hospitalized for said infection.

	Total population*			Infected patients			Hospitalized patients		
	551,320			41,603			22,362		
	Alive 540,069	Dead 11,251	*p*	Alive 30,392	Dead 11,251	*p*	Alive 13,828	Dead 8,534	*p*
Age (years)	83.1 ± 5.8	86.4 ± 5.9	<0.0001	84.1 ± 5.8	86.4 ± 5.9	<0.0001	83.9 ± 5.6	86.1 ± 5.8	<0.0001
Sex (% male)	38	53.1	<0.0001	38.5	53.1	<0.0001	45.2	54.6	<0.0001
Deprivation index			<0.0001			<0.0001			<0.0001
Less deprivation	28.5	24.3		26.3	24.3		22.7	22.2	
Low-medium deprivation	23.1	27.3		24.3	27.3		23.6	27.2	
Medium-high deprivation	25.1	25.5		24.5	25.5		26.0	26.8	
High deprivation	23.3	22.9		24.9	22.9		27.8	23.9	
Active cancer during the last 5 years (%)	5.2	7.4	<0.0001	5.2	7.4	<0.0001	5.9	7.4	<0.0001
Chronic liver disease (%)	1.0	1.2	0.008	1.1	1.2	0.127	1.2	1.3	0.306
Hypertension (%)	61.5	63.1	<0.0001	63.8	63.1	0.088	65	63.6	0.021
Diabetes (%)	23.5	30.7	<0.0001	26.8	30.7	<0.0001	29.1	31.4	<0.0001
Atrial fibrillation (%)	14.7	23.6	<0.0001	16.8	23.6	<0.0001	18.0	23.7	<0.0001
Thromboembolic disease (%)	3.7	6.0	<0.0001	4.6	6.0	<0.0001	5.2	6.1	<0.0001
Chronic renal failure (%)	6.0	9.6	<0.0001	6.7	9.6	<0.0001	7.9	9.8	<0.0001
Heart failure (%)	5.9	13.3	<0.0001	7.7	13.3	<0.0001	8.8	13.4	<0.0001
Chronic obstructive pulmonary disease or asthma (%)	10.3	15.0	<0.0001	12.6	15.0	<0.0001	15.3	15.6	0.293
Rheumatoid arthritis (%)	3.4	3.7	0.032	3.9	3.7	0.157	3.9	3.7	0.264
Alzheimer's disease (%)	7.8	17.0	<0.0001	12.5	17.0	<0.0001	10.8	15.7	<0.0001
Cardiovascular disease (%)	19.0	23.7	<0.0001	19.0	26.9	<0.0001	21.4	27.2	<0.0001
Stroke (%)	5.9	10.3	<0.0001	7.2	10.3	<0.0001	7.4	10.2	<0.0001
Myocardial infarction (%)	4.5	7.3	<0.0001	5.1	7.3	<0.0001	6.0	7.4	<0.0001
Angina (%)	4.5	6.5	<0.0001	5.2	6.5	<0.0001	5.7	6.6	0.004
Peripheral arterial disease (%)	4.3	7.8	<0.0001	5.0	7.8	<0.0001	5.9	7.9	<0.0001
Excessive alcohol consumption (%)	1.1	1.6	<0.0001	1.3	1.6	0.006	1.6	1.6	0.485
Tobacco use (%)	4.8	5.4	0.003	4.5	5.4	<0.0001	5.3	5.6	0.161
Body mass index (kg/m^2)	28.1 ± 4.7	28.1 ± 5.0	0.025	28.2 ± 4.8	28.1 ± 5.0	0.172	28.5 ± 4.9	28.2 ± 5.0	<0.0001

* 36,283 patients were excluded who died in 2020 and January 2021 due to causes that were not unequivocally attributable to COVID-19.

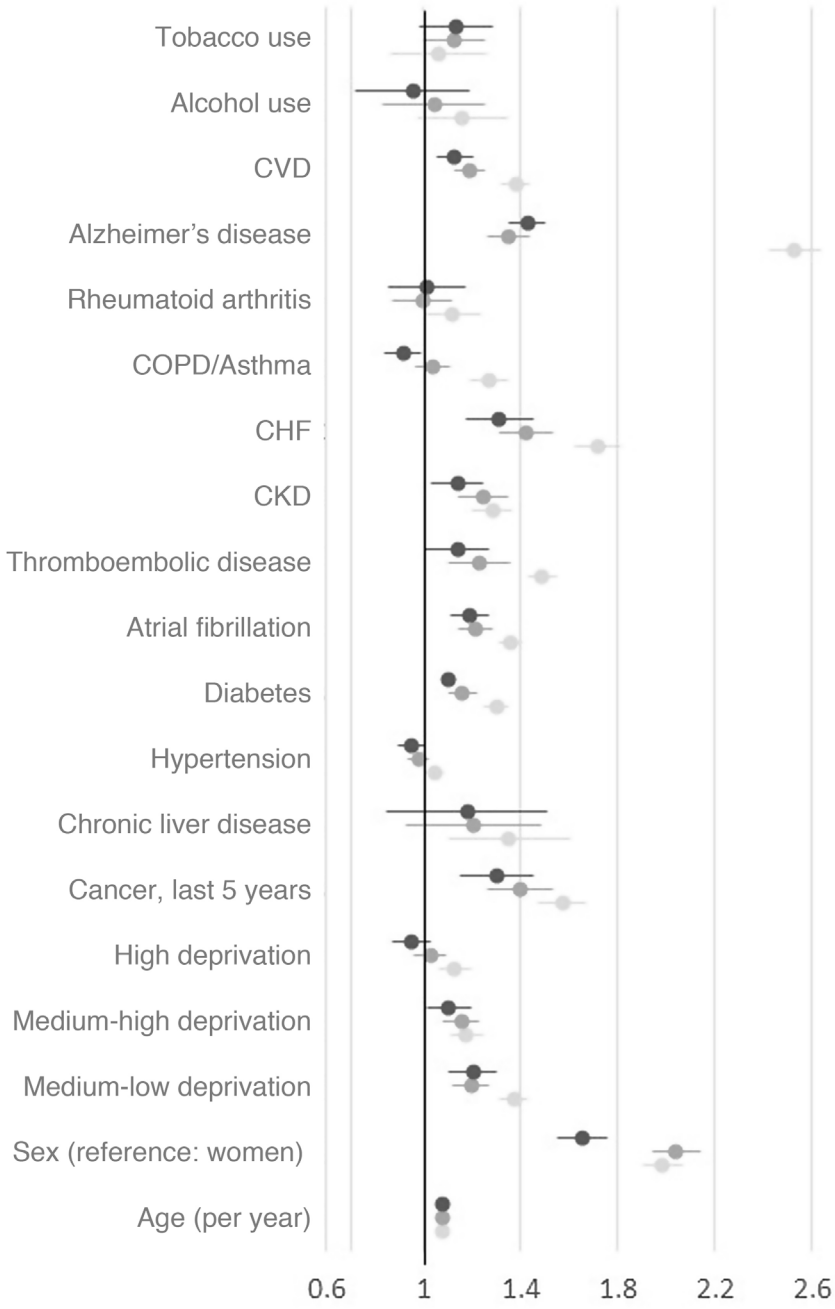

Figure 2 Multinomial logistic regression analysis (population older than 75 from the Community of Madrid (light gray)) and binary logistic regression analysis (infected patients (dark gray) and hospitalized patients (black)) of the factors associated with SARS-CoV-2 mortality, OR (95%CI).
CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease; CHF: chronic heart failure; CKD: chronic kidney disease.

year, mortality was more closely associated with the presence of cancer, liver disease, cardiovascular disease, chronic kidney disease, and, fundamentally, Alzheimer's disease.

Discussion

Our results demonstrate that one out of every 53 individuals older than 75 years who were residents in the CM died as a consequence of COVID-19 from 2020 to January 31, 2021. They also indicate that slightly more than one of every four infected patients and one of every three hospitalized patients died. The data do not include patients who died at home or in nursing homes with an unconfirmed infection or the numerous cases which survived the disease without it being confirmed.

Various studies have evaluated mortality due to COVID-19 in the general population,[3] which includes both the risk of becoming infected and the risk of dying from said infection in a single variable. This approximation does not allow for differentiating whether the greater mortality attributable

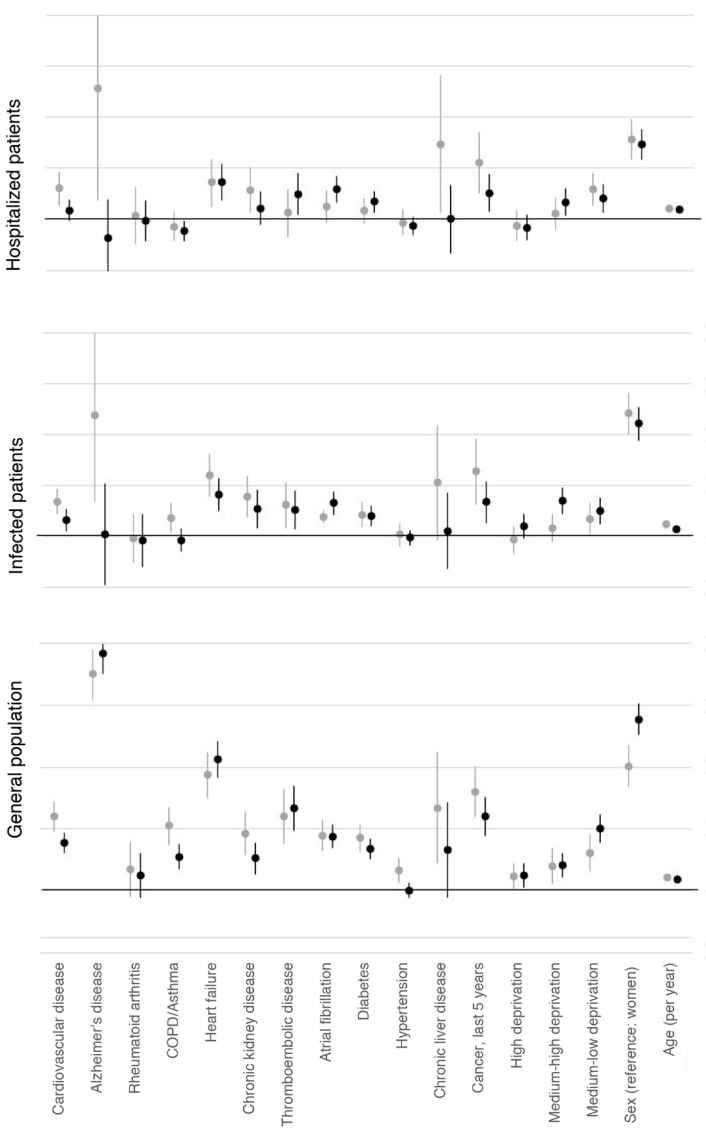

Figure 3 Factors associated with mortality during the first wave (before July 1, 2020, 7,466 deaths (black)) and subsequent waves (July 1, 2020 to January 31, 2021, 3,588 deaths (gray)) in the total Madrid population older than 75 years (587,603 subjects), in 41,603 subjects with confirmed SARS-CoV-2 infection, and in 22,362 patients hospitalized due to this infection.
COPD: chronic obstructive pulmonary disease.

to a certain risk factor is due to the fact that patients with that risk factor became infected more easily and, thus, their probability of dying is higher given this greater risk or if, once infected, the case fatality rate increases in those who have that specific factor. Likewise, other studies have evaluated risk of mortality in hospitalized patients,[8] focusing on a very specific segment of patients, namely those with progression of already-severe disease; this excludes individuals with mild disease who are not candidates for hospitalization.

This study analyzed mortality in different populations. Mortality was able to be evaluated in three population groups: the entire population of Madrid, infected individuals, and hospitalized individuals. This allowed for comparing our data with most studies which have evaluated mortality in any of these segments. Another important characteristic of this study is that the risk factors, diseases, and anthropometric measurements were obtained months before infection occurred.

The prevalence of chronic diseases and risk factors was greater in infected and hospitalized patients than in the general population, which allows for speculating about various possibilities. The first and most obvious is that these patients had a greater risk of becoming infected and developing a more severe infection because they had chronic diseases, either because they worsened the infection's progress or because the infection decompensated their disease. However, it cannot be ruled out that these patients came to the hospital earlier because they felt vulnerable and the physicians themselves considered them as such, favoring their admission. In this sense, the lower percentage of hospitalized patients with Alzheimer's disease compared to infected patients with Alzheimer's disease is of note. It is possible that many of them died before being transferred to the hospital or were transferred to provisional facilities set up for these patients instead of hospitals for their management during the first waves of the disease.

Age and male sex were associated in a very significant manner with mortality, both on the population level and in infected and hospitalized patients. The association between sex and mortality has consistently been found in all large series of patients with COVID-19 infection.[3] It has been attributed both to differences related to sex and to the different prevalence of some risk factors, such as tobacco use or diseases like COPD or coronary artery disease, though there are no studies which have clearly defined the cause. This study, in which the analyses were adjusted for many chronic diseases, shows that excess mortality due to COVID-19 in men was not only due to their greater morbidity.

The intensity of each risk factor's association with mortality declined in infected patients and hospitalized patients compared to what was observed in the general population. Infected and hospitalized patients had a greater prevalence of comorbidities, which would have diluted the effect of a specific disease, reducing the strength of the association. In this regard, it merits mention that though almost all chronic diseases were associated with greater mortality in the total population, hypertension, chronic liver disease, rheumatoid arthritis, and COPD were not associated with greater mortality among infected or hospitalized subjects. The higher mortality in patients with COPD has been questioned in some studies and in others, it has been demonstrated that it is not significant in older adult patients.[8,14–16] On the other hand, it has been described that the use of inhaled corticosteroids,[17,18] common in COPD, or systemic anti-inflammatory agents,[19,20] common in rheumatological diseases, could reduce mortality by lessening the exaggerated inflammatory response typical of this disease, though the data have not been conclusive.

The lower mortality of the population with less deprivation, that is, the population with a higher socioeconomic status, has already been described.[21] Subjects with less deprivation were more represented in the total population, but this percentage declined when only infected and hospitalized patients were considered. On the contrary, subjects with greater deprivation represented a higher percentage of infected and hospitalized patients, indicating a higher rate of infection and hospitalization. Upon correcting for the different risk factors, the differences declined, though a lower mortality rate remained significant in populations with a higher socioeconomic status, indicating that the differences are not due to a different chronic disease burden. Differences in mortality were smaller in hospitalized patients, which indicates that once admitted, prognosis is less dependent on socioeconomic level and tends to become equal.

Mortality was greater during the first part of the pandemic despite many deaths not being recorded, given that there were no diagnostic tests available to confirm the infection. This hinders comparing population mortality and the case fatality rate between both periods. However, it is possible to compare mortality in hospitalized patients, which was lower during the second wave (41.2% vs. 33.4%). It cannot be ruled out that the lower pressure on the healthcare system—the peak of admissions was 14,000 in the first wave versus 3,500 in the second[22]—led to a greater number of less severe patients being admitted in the second period. However, this seems improbable given that the profile of hospitalized patients did not notably differ between both periods. It is likely that better clinical management in this second part of the pandemic led to a better prognosis. Likewise, during the first wave, there was also greater mortality outside of the hospital, namely in nursing homes and the provisional facilities set up to care for these patients.

Limitations of the study

The limitations of this study arise from difficulties in establishing the diagnosis of an infection during the first phase of the pandemic. Many patients died outside the hospital without a confirmed diagnosis, which led to an underestimated mortality rate. In turn, many patients who had mild infection were not diagnosed because PCR tests were not available except for in the hospital. Therefore, the incidence of infection was also underestimated. During the first wave of the pandemic, the majority of patients who were diagnosed were those who came to the hospital, the only place where PCR tests were available and as such, they were the most severe cases of COVID-19. Lastly, our results refer exclusively to the public healthcare system.

Data from the 2020 national seroprevalence program indicated an overall rate of SARS-CoV-2 IgG antibodies of 18.6%, a rate which was higher in women (19.9%) than in men (17.1%), but with no notable differences in regard to

age groups. This implies that there should have been approximately 110,000 subjects, 38,800 men and 72,000 women, infected at the end of 2020, a much higher figure than the 41,000 confirmed cases in this study.[23] It is evident that many cases are asymptomatic and that, in many other instances, patients did not go to the doctor due to the inherent difficulties in the beginning of the pandemic.

The factors found in our study are those regarding the first waves of the pandemic and could have changed with vaccination and the arrival of new virus variants.

The strength of this study comes from its large sample size, which allows for drawing valid comparative conclusions regarding the factors associated with risk of infection, hospitalization, and death, and that it included nearly all cases which occurred in the CM in 2020.

In conclusion, mortality in subjects older than 75 years in the CM during the first year of the pandemic was very high. Age, male sex, and numerous comorbidities were associated with risk of death due to COVID-19. Mortality in hospitalized patients declined notably during the second part of the year.

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Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rce.2022.06.002.

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