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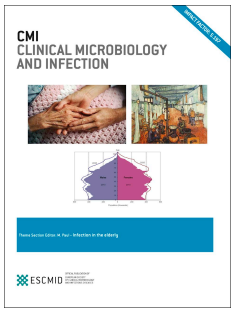

Characteristics and predictors of death among 4,035 consecutively hospitalized patients with COVID-19 in Spain

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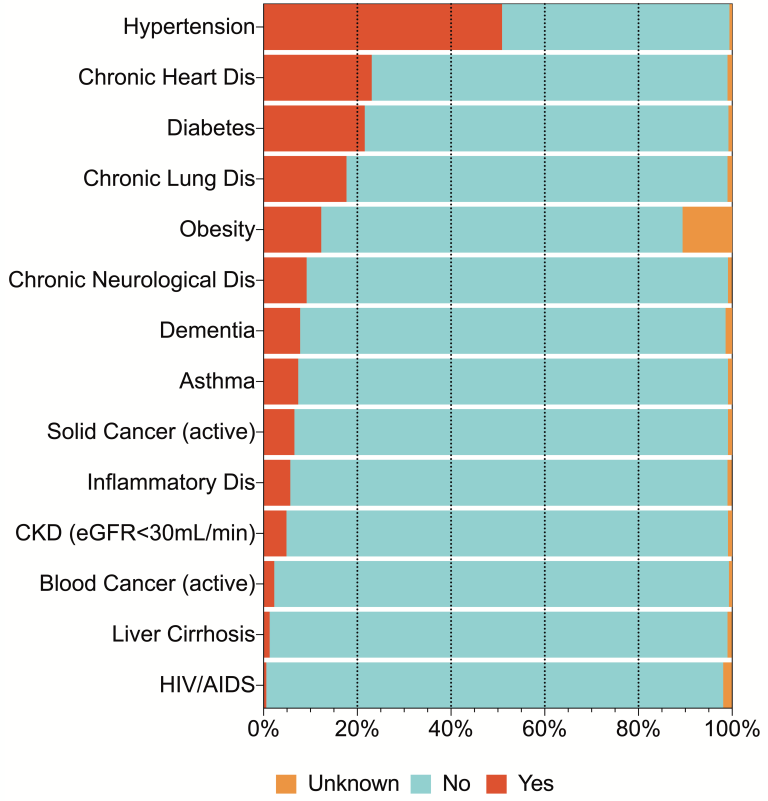
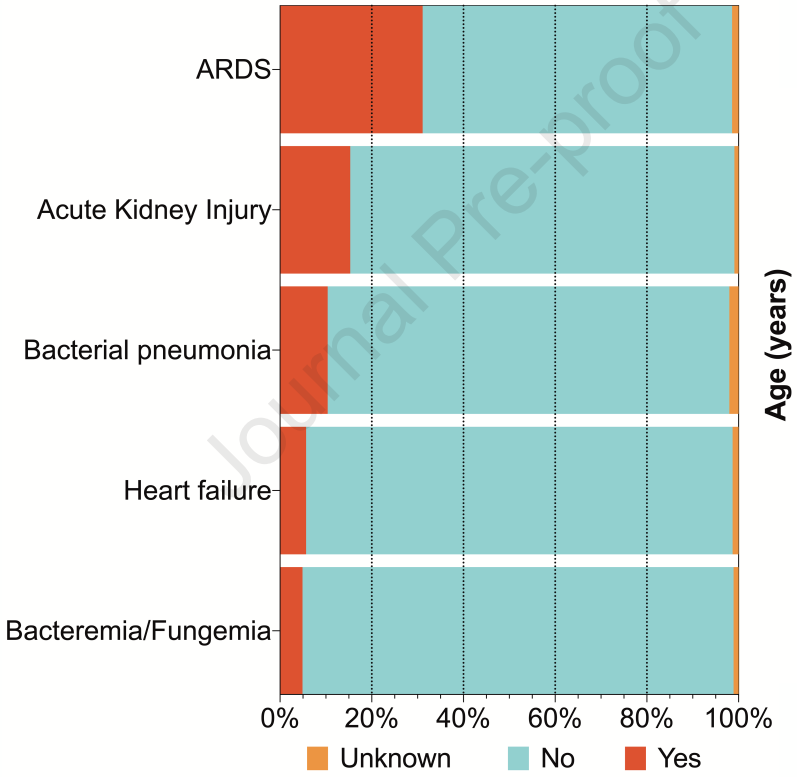
CHARACTERISTICS AND PREDICTORS OF DEATH AMONG 4,035 CONSECUTIVELY HOSPITALIZED PATIENTS WITH COVID-19 IN SPAIN

- 4,035 consecutive patients with COVID-19 (RT-PCR +) admitted to 127 hospitals until 17-03-2020.
- ♂ 61%, Median (IQR) age 70 (56–80) years; 25% ≥ 80 years
- 73.8% ≥ 1 comorbidity and 26.7% ≥ comorbid conditions

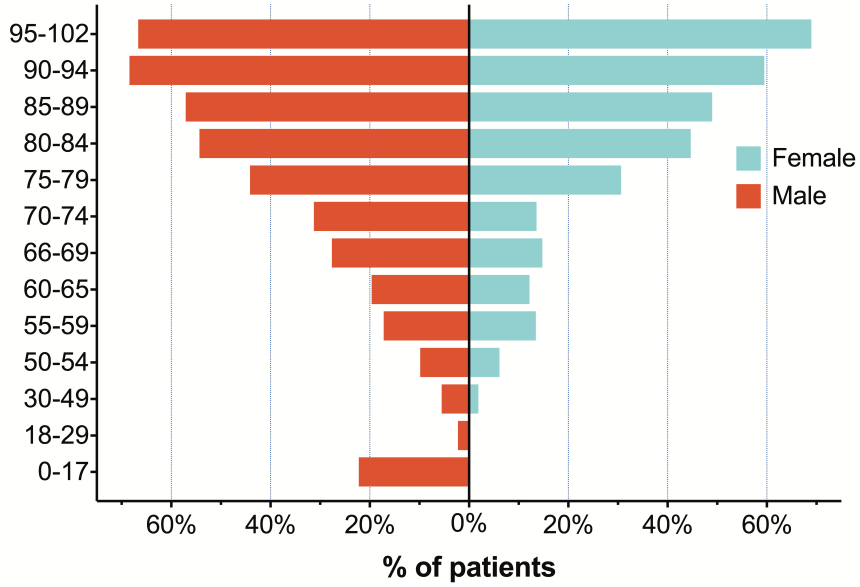
Comorbidities



Complications (>4%)



Mortality stratified by age and sex



Outcome	• Death = 28.0% • Discharged alive = 64.1% • Hospitalized = 7.8%	**Mortality in Subgroups**	• ARDS = 59.3% • ≥ 80 years = 54.9% • ≥ 3 comorbidities = 47.7% • Mechanical ventilation = 45.7% • ICU = 42.4%

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Original article

Characteristics and Predictors of Death among 4,035 Consecutively Hospitalized Patients with COVID-19 in Spain

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*Contributed equaly to this work

Keywords

SARS-CoV-2, COVID-19, Coronavirus

Running title: Severe COVID-19 in Spain

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Abstract

Objectives

We aimed to analyse the characteristics and predictors of death in hospitalized patients with COVID-19 in Spain.

Methods

Retrospective observational study of the first consecutive patients hospitalized with COVID-19 confirmed by real-time polymerase chain reaction (RT-PCR) assay in 127 Spanish centres until March 17, 2020. The follow-up censoring date was April 17, 2020. We collected demographic, clinical, laboratory, treatment, and complications data. The primary endpoint was all-cause mortality. Univariable and multivariable Cox regression analyses were performed to identify factors associated with death.

Results

Of the 4,035 patients, males accounted for 2,433/3,987 (61.0%), the median age was 70 years, and 2,539/3,439 (73.8%) had ≥1 comorbidity. The most common symptoms were a history of fever, cough, malaise, and dyspnoea. During hospitalization 1,255/3,979 (31.5%) patients developed acute respiratory distress syndrome, 736/3,988 (18.5%) were admitted to intensive care units, and 619/3,992 (15.5%) underwent mechanical ventilation. Viral or host-targeted medications included lopinavir/ritonavir 2,820/4,005 (70.4%), hydroxychloroquine 2,618/3,995 (65.5%), interferon-beta 1,153/3,950 (29.2%), corticosteroids 1,109/3,965 (28.0%), and tocilizumab 373/3,951 (9.4%). Overall 1,131/4,035 (28%) patients died. Mortality increased with age (85.6% occurring in older than 65 years). Seventeen factors were independently associated with an

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63 increased hazard of death, the strongest among them included advanced age, liver cirrhosis, low
64 age-adjusted oxygen saturation, higher concentrations of C-reactive protein, and lower estimated
65 glomerular filtration rate.

66 ## Conclusions

67 Our findings provide comprehensive information about characteristics and complications of
68 severe COVID-19 and may help to identify patients at a higher risk of death.

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Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) associated coronavirus disease 2019 (COVID-19) emerged in China in December 2019 and has spread globally, creating a worldwide pandemic and a public health crisis of historical dimension (1). The clinical spectrum of COVID-19 varies widely, from asymptomatic disease to pneumonia and life-threatening complications, including acute respiratory distress syndrome (ARDS), multisystem organ failure, and, ultimately, death (2-4).

Several case series or cohorts describing the clinical characteristics and outcomes of patients with severe COVID-19 have been reported summarizing the experience of city or regional hospitals in China (2, 5, 6), Singapore (7) or New York City (8, 9); as well as case series of critically ill patients admitted to intensive care units (ICUs) in China (10), Italy (4) or the US (11). However, variations in the rates for COVID-19 hospitalizations and deaths may occur across different areas even in the same country suggesting differences in population characteristics or inequities in the access to care (12). We are aware of three prior published nationwide cohorts of hospitalized patients with COVID-19, two from China (3, 13) and one from United Kingdom (14). None of these three cohorts explored both clinical and laboratory variables associated with hospital death.

Our study aims to determine the epidemiological and clinical characteristics of hospitalized patients with COVID-19 in Spain and to identify clinical and laboratory predictors of death.

Patients and Methods

Design and Patient Selection

COVID-19@Spain is a retrospective nationwide cohort study of patients admitted to Spanish hospitals with laboratory-confirmed COVID-19 infection by real-time polymerase chain reaction (RT-PCR) assay for SARS-CoV-2. Investigators from participating centres were asked to include the first consecutive hospitalized patients (up to 100) meeting the study criteria from the start of the epidemic in Spain until March 17, 2020. The Ethics Committee for Research with Medicines of Hospital General Universitario Gregorio Marañón approved the study and waived informed consent for the collection of clinical data.

Investigations

The data source was the electronic medical records. All data were collected using an electronic case report form (eCRF), a modified version of the WHO–International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) Core CRF (15). The eCRF was built using REDCap electronic data capture tools (16), and hosted at SEIMC (Spanish Society of Infectious Diseases and Clinical Microbiology)/GESIDA (AIDS Study Group) Foundation (FSG).

The variables registered included administrative data, epidemiological information, and type of clinical specimen in which the diagnosis was confirmed. We also registered demographics, comorbidities, current medications, signs and symptoms at admission, baseline laboratory tests results, chest radiographic findings at baseline and during follow-up, development of ARDS and other complications during hospitalization, use of medications with purported activity against COVID-19, use of adjunctive medications to modulate the host inflammatory response, admission to a high dependency unit or ICU, non-invasive ventilation, mechanical ventilation, use of extracorporeal membrane oxygenation (ECMO), vasopressor agents and renal replacement therapy.

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The clinical status of the patients as of April 17, 2020, was categorized as discharged alive (with the date of discharge), alive and currently hospitalized, or dead (with the date of death). For patients who were discharged and subsequently readmitted during the study period, only one hospital admission episode was considered for purposes of analysis.

Outcome

The primary endpoint was all-cause mortality. Baseline was the date of hospital admission. The follow-up censoring date was April 17, 2020.

Definitions

Comorbidities and complications during hospitalization were defined as diagnoses included in the medical record. Cancer was defined as the presence of an active solid or hematologic malignant neoplasm. Obesity was defined as a body mass index (BMI) > 30. ARDS was defined as the acute onset or worsening of respiratory symptoms with severe hypoxemia and bilateral opacities on chest radiograph not fully explained by cardiac failure or fluid overload (17).

Study oversight

The investigators of each participating centre vouch for the completeness and accuracy of the data. FSG monitors maintained close contact with investigators for problem resolution during the period of data retrieval; they checked the database for missing, invalid, and inconsistent data; and managed queries before the analysis.

Statistical analysis

Univariable and multivariable Cox regression analyses were performed to identify factors associated with death. To obtain a reduced set of variables from the broad set of predictors, we

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carried out a block-wise forward procedure allocating the predictor variables into five clusters: sociodemographic characteristics, comorbidities, admission signs and symptoms, vital signs, and laboratory parameters. A multivariable regression analysis was fitted within each block using two criteria to achieve the best set of predictors: relevance to the clinical situation and statistical significance (P<0.10). We used variance inflation factors to detect collinearity among predictors included in the multivariable models. We carried out a sensitivity analysis in which the order of entry of the blocks was inverted. We checked the proportional hazards assumption. Variables with more than 25% of missing values have not been considered, and missing values were treated as a separate category for analysis. Heterogeneity introduced by different hospitals was accounted for by using robust methods to estimate standard errors and, thus, to calculate 95% confidence intervals (CI) and *P*-values. Statistical analyses were done using Stata software (version 15.0; Stata Corporation, College Station, Texas, USA. This study is registered with ClinicalTrials.gov, NCT04355871.

Results

The final cohort included 4,035 hospitalized patients (**see web-only Supplementary Figure S1**) in which SARS-CoV-2 was detected by RT-PCR (nasopharyngeal swabs [89.6%], pharyngeal swabs [13.4%], low respiratory tract specimens [1.3%], and other specimens [4.4%]. The median admission date was 13 March 2020, with little variability among the median admission date between the centres (range from 6 to 17 March). The median follow-up time was 34 days (interquartile range [IQR] 24 – 37 days). A total of 141 patients (3.6%) were discharged and readmitted during the study period, a median time of 5 days (IQR 2 – 9 days) after discharge.

Demographics and presenting clinical features

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Patients' characteristics, categorized by survival, are shown in **Table 1**. In brief, males accounted for 61.0%, the median age was 70 years, and 25.1% were ≥ 80 years old. Most patients were Spanish born whites. The age distribution of patients stratified by sex is shown in **Figure 1A**.

At least one comorbidity was present in 73.8% and 26.7% had at least three comorbid conditions. The most common comorbidities were arterial hypertension (51.2%), chronic heart disease (23.3%), diabetes mellitus (21.8%), chronic pulmonary disease (not asthma) (17.9%), and obesity (13.8%). Only 0.7% of patients had HIV. Before admission, 19.4% patients were on angiotensin-converting enzyme (ACE) inhibitors, and 17.3% were receiving angiotensin II receptor blockers (ARBs) (**Table 1**).

The median duration of symptoms before hospitalization was 4 (IQR 2 – 7) days, and the most commonly reported were history of fever (81.0%), cough (71.8%), malaise (64.0%), dyspnoea (49.1%), upper respiratory tract symptoms (30.8%), myalgia or arthralgia (24.9%), and sputum production (24.1%) (**see web-only Supplementary Table S2**). Abnormal vital signs at admission included fever (40.9%), arterial hypotension (18.8%), and marked tachypnoea (10.9%). Low age-adjusted SaO_2 levels on room air were reported in 26.6% of patients (**see web-only Supplementary Table S3**).

Chest radiograph findings

Infiltrates on initial chest radiograph were observed in 77.6% patients, of which 71.3% had bilateral involvement. Over the whole hospital course, worsening of the baseline infiltrates was observed in 64.7% of patients, with new lesions in 51.0%.

Laboratory findings

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Baseline laboratory findings are shown in **Table 2**. The most common abnormalities in blood counts included lymphopenia (54.2%) and thrombocytopenia (31.5%). The median (IQR) neutrophil-to-lymphocyte ratio was 4.5. A prolonged activated partial thromboplastin time (APTT) was present in 9.4%, and 57.1% had D-Dimer levels above the normal range. High serum levels were reported from alanine aminotransferase (ALT) (25.3%), aspartate aminotransferase (AST) (34.7%), LDH (64.5%), creatine kinase (CK) (23.5%), CRP (91.9%), and procalcitonin (14.2%). Low serum albumin was found in 36.0% patients, and 6.8% had an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2 by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Ferritin and interleukin-6 (IL-6) were determined in a limited number of patients, and high concentrations of these parameters were found in 75.1% and 90.0%, respectively.

Supportive therapy and medications

High dependency unit or ICU admission was required for 18.5% patients, 15.5% underwent mechanical ventilation, 11.9% received vasopressors, and 3.0% received renal-replacement therapy (**see web-only Supplementary Table S4**)**.** Viral targeted agents were administered to 82.0% of patients: lopinavir/ritonavir (LPV/r) (70.4%), hydroxychloroquine (65.5%), and subcutaneous interferon-beta (29.2%), usually in combination with LPV/r. Host-targeted agents included systemic corticosteroids in 28.0% patients and tocilizumab in 9.4% patients. Antibiotics other than azithromycin were administered to 80.9% patients and antifungals to 3.2% (**see web-only Supplementary Table S5**).

Complications and mortality

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The full list of complications during the hospital course is shown as supplementary material (**see web-only Supplementary Table S6**); the most common were ARDS (31.5%), acute kidney injury (15.4%), presumed bacterial pneumonia (10.6%), heart failure (5.8%), and blood-stream infection (4.9%). During the study period, 28.0% of patients died, 64.1% were discharged, and 7.8% remained hospitalized. The median (IQR) time to death since the beginning of symptoms and since hospital admission was 13 (9-19) days and 10 (6-16) days, respectively. Death was particularly high among patients ≥ 80 years (54.9%) (**Figure 1B**) and those with ≥3 comorbid conditions (47.7%). Death was also very high among those with ARDS (59.3%), those who were admitted to ICU (42.4%), and those who underwent mechanical ventilation (45.7%). The median (IQR) length of stay was 4 (1-9) days for patients who were discharged; and 35 (32-38) days for those who remained hospitalized at the censoring date.

Predictors of death

Independent predictors of death in the different clusters of variables are shown in **Table 3**. In the final adjusted analysis, we found 17 factors independently associated with an increased hazard of death: male sex, older age, arterial hypertension, obesity, liver cirrhosis, chronic neurological disorder, active cancer, dementia, dyspnoea, confusion, low age-adjusted SaO_2 on room air, higher white cell blood count (WBC), higher neutrophil-to-lymphocyte ratio, lower platelet count, prolonged INR, lower eGFR, and higher concentrations of CRP (**Figure 2**). No collinearity was detected, the proportional hazards assumption was fulfilled, and the results were not changed when the order of entry of the blocks was inverted. Kaplan-Meier plots for death according to age and sex are shown in **Figure 3**. The adjusted hazard ratio (aHR) of death for being admitted early in the epidemic (before 13 March) vs later was 1.07 (95% confidence interval [CI]: 0.90; 1.28),

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P=0.407. The variable unilateral or bilateral lung opacities had missing values in 29% individuals and was not included in the final model. However, when this variable was included in the model, the aHR (95%CI) of death for bilateral opacities in comparison with unilateral opacities was 1.32 (0.11; 1.55) P=0.002. We also carried out two post-hoc analyses (data not shown). In the first one, the predictors of mortality among patients ≤ 65 years were not substantially different from those found in the whole data set. In the second analysis, the mortality hazard did not change depending on the seroprevalence of IgG anti-SARS-Cov2 at the provincial level, according to a recent nationwide study in Spain. (18).

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Discussion

This cohort describes the presenting characteristics and outcomes of 4,035 patients with COVID-19 admitted to 127 centres in Spain during the first month of the country outbreak. We are aware of three prior published nationwide cohorts of hospitalized patients with COVID-19, two from China (3, 13) and one from UK. The majority of patients in all four cohorts were male. However, in comparison with Chinese patients, those from Spain and the UK were on average, two decades older and had a prevalence three times higher of comorbid conditions. It is not surprising thus that mortality was substantially higher in Spain (28%) and the UK (26%) than China (1.4 and 3.2%). Presenting features were similar in all cohorts. However, dyspnoea was less frequent in Chinese patients suggesting a more severe course in the older Spanish and British patients. In our cohort, age was the main determinant of death, as has been in other series of hospitalized patients with COVID-19 (3, 8, 9, 14, 19). Independently of the higher prevalence of comorbidities, it cannot be ruled out that older patients could not have been prioritized to receive ICU treatment. Death was also significantly higher among men than in women, as has also been described in other cohorts (3, 8, 9, 13, 14). There are sex differences in innate and adaptive immune responses that might have an impact on the inflammatory response and outcomes of COVID-19 and deserve further investigation (20). Hypertension was not only the most common comorbidity in our cohort, as in other studies, but also an independent predictor of mortality. The association between hypertension and poor outcomes in COVID-19 does not seem to be simply a matter of high prevalence; alternative explanations include pre-existing hypertensive end-organ or endothelial damage and interactions between COVID-19 and antihypertensive medications (21). Many patients with hypertension were receiving ACE inhibitors or ARBs, but they did not increase

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mortality. Obesity was the fifth most common comorbidity in our cohort but one with the highest hazard of mortality. Obesity has been found to increase the risk of hospitalization and severe outcomes during influenza seasons (22). Recent studies with COVID-19 patients indicate that younger hospitalized individuals were more likely to be obese (23) and that obesity is associated with severe pictures (23-25) and increased mortality (14). Other underlying conditions associated with an increased hazard of death were active cancer and cirrhosis and as has been reported elsewhere (26, 27); meaning that clinicians should consider patients with these underlying conditions as a high-risk category for COVID-19 (27). We identified several routine laboratory markers as predictors of mortality, including the neutrophil-to-lymphocyte ratio, an indicator of systemic inflammation that has been found of prognostic utility in sepsis (28), and COVID-19 (29, 30).

Our study is limited by the retrospective design and the high number of sites, which might have jeopardized the quality of the data. We tried to solve this by selecting simple and well-defined variables and by careful monitoring of the data. Admission criteria might have differed between the sites; nevertheless, we controlled the site effect in the analysis. We could not include in the multivariable model some potentially interesting laboratory parameters, nor changes in laboratory findings over time. The study's strengths include the large sample size, which allowed the identification of a high number of predictors of death at admission, the analysis of clinical and laboratory variables, and the inclusion of sites from areas with different incidence rates.

In summary, here we report the clinical characteristics of a large cohort of patients with COVID-19 consecutively admitted to hospitals in Spain during the first month of the epidemic. Our findings provide comprehensive information about characteristics and complications of severe COVID-19 and may help to identify patients at hospital admission with a higher risk of death.

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Transparency declaration

Disclosures

Juan Berenguer reports grants and personal fees from ABBVIE, grants and personal fees from GILEAD, grants and personal fees from MSD, grants and personal fees from ViiV Healthcare, personal fees from JANSSEN outside the submitted work.

Pablo Ryan reports personal fees from AbbVie, grants and personal fees from GILEAD, personal fees from JANSSEN, grants from MSD, personal fees from ViiV Healthcare, outside the submitted work.

Inmaculada Jarrín reports personal fees from GILEAD, personal fees from ViiV Healthcare, outside the submitted work.

José R Arribas reports grants and personal fees from ALEXA, grants and personal fees from GILEAD, grants and personal fees from MSD, grants and personal fees from JANSSEN, grants and personal fees from SERONO, grants and personal fees from TEVA, grants and personal fees from ViiV Healthcare, outside the submitted work.

José R Baño, Jordi Carratalà, Maria Yllescas, and Jerónimo Pachón have nothing to disclose.

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Acknowledgements

Members of the COVID-19@Spain Study Group that have made substantial contributions by data collection are listed in the Appendix

Contribution

Conception of the work: Juan Berenguer and José R Arribas.

Design of the database: Juan Berenguer, Pablo Ryan, María Yllescas, and José R Arribas.

Analysis of data: Inmaculada Jarrín.

Interpretation of data: All authors.

Drafting of the manuscript: Juan Berenguer.

Critical revision of the manuscript for important intellectual content: All authors.

Final approval of the manuscript: All authors.

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors

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References

1. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270-3.

2. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.

3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020.

4. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020.

5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

6. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091.

7. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. JAMA. 2020.

8. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020.

Journal Pre-proof

333 9. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of
334 Covid-19 in New York City. N Engl J Med. 2020.

335 10. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill
336 patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective,
337 observational study. Lancet Respir Med. 2020.

338 11. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al.
339 Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City:
340 a prospective cohort study. The Lancet. 2020;395(10239):1763-70.

341 12. Wadhera RK, Wadhera P, Gaba P, Figueroa JF, Joynt Maddox KE, Yeh RW, et al. Variation in
342 COVID-19 Hospitalizations and Deaths Across New York City Boroughs. JAMA. 2020.

343 13. Liang WH, Guan WJ, Li CC, Li YM, Liang HR, Zhao Y, et al. Clinical characteristics and
344 outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei
345 (non-epicenter): A Nationwide Analysis of China. Eur Respir J. 2020.

346 14. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20
347 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation
348 Protocol: prospective observational cohort study. BMJ. 2020;369:m1985.

349 15. WHO–International Severe Acute Respiratory and Emerging Infections Consortium
350 (ISARIC). Core Case Record Form - Severe Acute Respiratory Infection,Version 7JAN16.
351 https://media.tghn.org/medialibrary/2016/06/ISARIC-WHO-
352 SARI_Case_Record_Form_7JAN16.pdf2016.

Journal Pre-proof

16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81.

17. The ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526-33.

18. Ministerio de Sanidad. Estudio Nacional de Sero-Epidemiología de la Infección por SARS-Cov-2 En España. Informe Preliminar 13 de Mayo de 2020. https://www.mscbs.gob.es/ciudadanos/ene-covid/docs/ESTUDIO_ENE-COVID19_PRIMERA_RONDA_INFORME_PRELIMINAR.pdf. 2020.

19. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62.

20. Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626-38.

21. Schiffrin EL, Flack JM, Ito S, Muntner P, Webb RC. Hypertension and COVID-19. Am J Hypertens. 2020;33(5):373-4.

22. Kwong JC, Campitelli MA, Rosella LC. Obesity and respiratory hospitalizations during influenza seasons in Ontario, Canada: a cohort study. Clin Infect Dis. 2011;53(5):413-21.

23. Kass DA, Duggal P, Cingolani O. Obesity could shift severe COVID-19 disease to younger ages. The Lancet. 2020;395(1474-547X (Electronic)):1544-5.

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373 24. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in patients
374 younger than 60 years is a risk factor for Covid-19 hospital admission. Clin Infect Dis. 2020.

375 25. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, et al. High prevalence
376 of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive
377 mechanical ventilation. Obesity (Silver Spring). 2020.

378 26. Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact
379 of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet. 2020;395(10241):1907-18.

380 27. Singh S, Khan A. Clinical Characteristics and Outcomes of COVID-19 Among Patients with
381 Pre-Existing Liver Disease in United States: A Multi-Center Research Network Study.
382 Gastroenterology. 2020.

383 28. Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in
384 sepsis: A meta-analysis. Am J Emerg Med. 2020;38(3):641-7.

385 29. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein
386 ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol.
387 2020.

388 30. Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HHX, et al. Neutrophil-to-lymphocyte ratio as an
389 independent risk factor for mortality in hospitalized patients with COVID-19. J Infect. 2020.

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391

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Figure Legends

Figure 1.

Distribution of hospitalized patients with COVID-19 stratified by age and sex (A). Mortality of patients with COVID-19 stratified by age and sex (B)

Figure 2.

Univariable (A) and multivariable (B) Cox proportional hazards model of variables associated with death.

Abbreviations: WBC, white blood cell count; N/L, neutrophil-to-lymphocyte; INR, international normalized ratio; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein.

Figure 3.

Kaplan-Meier plots for death according to age (A) and sex (B)

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Appendix. The COVID-19@Spain Study Group.

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Table 1. Demographics, comorbidity data, and current medications of 4,035 hospitalized patients with COVID-19 stratified according to vital status at study censoring date

Characteristic	Alive (No.=2,904)	Death (No.=1,131)	P value	Total (No.=4,035)
Sex – No./total No. (%)			<0.001	
Male	1,666/2,868 (58.1)	767/1,119 (68.5)		2,433/3,987 (61.0)
Female	1,202/2,868 (41.9)	352/1,119 (31.5)		1,554/3,987 (39.0)
Pregnant female – No./with data (%)	13/1,136 (1.1)	2/329 (0.6)	0.395	15/1,465 (1.0)
Median gestational week (IQR)	33 (17 – 38)	-		33 (17 – 38)
Age				
Median (IQR) – yr.	65 (51 – 75)	79 (71 – 86)	<0.001	70 (56 – 80)
Distribution – No./with data (%)			<0.001	
0 – 10 yr.	13/2,901 (0.4)	2/1,130 (0.2)		15/4,031 (0.4)
11 – 20 yr.	18/2,901 (0.6)	0/1,130 (0)		18/4,031 (0.5)
21 – 30 yr.	89/2,901 (3.1)	2/1,130 (0.2)		91/4,031 (2.3)
31 – 40 yr.	210/2,901 (7.2)	5/1,130 (0.4)		215/4,031 (5.3)
41 – 50 yr.	373/2,901 (12.9)	18/1,130 (1.6)		391/4,031 (9.7)
51 – 60 yr.	483/2,901 (16.6)	68/1,130 (6.0)		551/4,031 (13.7)
61 – 70 yr.	624/2,901 (21.5)	167/1,130 (14.8)		791/4,031 (19.6)
71 – 80 yr.	675/2,901 (23.3)	357/1,130 (31.6)		1,032/4,031 (25.6)
81 – 90 yr.	355/2,901 (12.2)	389/1,130 (34.4)		744/4,031 (18.5)
≥ 91 yr.	61/2,901 (2.1)	122/1,130 (10.8)		183/4,031 (4.5)
Country of birth – No./with data (%)			<0.001	
Spain	2,505/2,819 (88.9)	1,065/1,101 (96.7)		3,570/3,920 (91.1)

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Other	314/2,819 (11.1)	36/1,101 (3.3)		350/3,920 (8.9)
Ethnic group – No./with data (%)			<0.001	
Arab	21/2,821 (0.7)	3/1,094 (0.3)		24/3,915 (0.6)
Asian	16/2,821 (0.6)	2/1,094 (0.2)		18/3,915 (0.5)
Black	12/2,821 (0.4)	0		12/3,915 (0.3)
Latin American	166/2,821 (5.9)	20/1,094 (1.8)		186/3,915 (4.7)
White	2,578/2,821 (91.4)	1,064/1,094 (97.3)		3,642/3,915 (93.0)
Other	28/2,821 (1.0)	5/1,094 (0.5)		33/3,915 (0.8)
Comorbidity				
Smoking history – No./with data (%)			<0.001	
Current smoker	134/2,123 (6.3)	63/794 (7.9)		197/2,917 (6.7)
Former smoker	613/2,123 (28.9)	334/794 (42.1)		947/2,917 (32.5)
Never smoked	1,376/2,123 (64.8)	397/794 (50.0)		1,773/2,917 (60.8)
Comorbid conditions – No./with data (%)			<0.001	
None	848/2,501 (33.9)	52/938 (5.5)		900/3,439 (26.2)
1-2	1,172/2,501 (46.9)	448/938 (47.8)		1,620/3,439 (47.1)
≥3	481/2,501 (19.2)	438/938 (46.7)		919/3,439 (26.7)
Types of comorbid conditions – No./with data (%)				
Hypertension	1,251/2,885 (43.4)	801/1,125 (71.2)	<0.001	2,052/4,010 (51.2)
Chronic heart disease	488/2,875 (17.0)	444/1,119 (39.7)	<0.001	932/3,994 (23.3)
Diabetes	514/2,884 (17.8)	357/1,118 (31.9)	<0.001	871/4,002 (21.8)
Chronic pulmonary disease (not asthma)	405/2,879 (14.1)	310/1,116 (27.8)	<0.001	715/3,995 (17.9)
Obesity	316/2,618 (12.1)	181/988 (18.3)	<0.001	497/3,606 (13.8)
Chronic neurological disorder	203/2,886 (7.0)	170/1,116 (15.2)	<0.001	373/4,002 (9.3)

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Dementia	124/2,871 (4.3)	191/1,108 (17.2)	<0.001	315/3,979 (7.9)
Asthma	230/2,884 (8.0)	69/1,116 (6.2)	0.053	299/4,000 (7.5)
Solid neoplasm (active)	146/2,882 (5.1)	121/1,116 (10.8)	<0.001	267/3,998 (6.7)
Inflammatory disease	148/2,883 (5.1)	83/1,114 (7.4)	0.005	231/3,997 (5.8)
Chronic kidney disease stage 4 (eGFR < 30 mL/min/1.73 m^2)	87/2,882 (3.0)	112/1,118 (10.0)	<0.001	199/4,000 (5.0)
Hematologic neoplasm (active)	45/2,885 (1.6)	47/1,120 (4.2)	<0.001	92/4,005 (2.3)
Liver Cirrhosis	28/2,882 (1.0)	26/1,116 (2.3)	0.001	54/3,998 (1.3)
HIV/AIDS	20/2,860 (0.7)	6/1,102 (0.5)	0.589	26/3,962 (0.7)
Current medications – No./with data (%)				
Angiotensin converting enzyme inhibitors	489/2,878 (17.0)	283/1,105 (25.6)	<0.001	772/3,983 (19.4)
Angiotensin II receptor blockers	434/2,879 (15.1)	254/1,108 (22.9)	<0.001	688/3,987 (17.3)
Corticosteroids inhaled	303/2,875 (10.5)	184/1,110 (16.6)	<0.001	487/3,985 (12.2)
Corticosteroids systemic	113/2,872 (3.9)	95/1,110 (8.6)	<0.001	208/3,982 (5.2)
Antineoplastic agents	59/2,875 (2.0)	49/1,110 (4.4)	<0.001	108/3,985 (2.7)
Biologic anti-inflammatory drugs	69/2,871 (2.4)	27/1,106 (2.4)	0.944	96/3,977 (2.4)
Antiretroviral drugs	15/19 (78.9)	6/6 (100.0)	0.220	21/25 (84.0)

Abbreviations: IQR, interquartile range; eGFR, estimated glomerular filtration rate

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Table 2. Laboratory findings of 4,035 hospitalized patients with COVID-19 stratified according to vital status at study censoring date

Laboratory parameter	**Alive (No.=2,904)**	**Death (No.=1,131)**	**P value**	**Total (No.=4,035)**
Haemoglobin				
Patients – No. with data	2,860	1,120		3,980
Median (IQR) – g/L	13.8 (12.6 – 14.9)	12.9 (11.5 – 14.4)	<0.001	13.6 (12.3 – 14.8)
Haematocrit				
Patients – No. with data	2,832	1,105		3,937
Median (IQR) – %	41.0 (37.9 – 44.0)	39.1 (34.8 – 43.0)	<0.001	40.6 (37.0 – 44.0)
WBC count				
Median (IQR) – cells/ $x10^9$/L	5,635 (4,330 – 7,420)	6,900 (5,000 – 9,470)	<0.001	5,910 (4,490 – 7,990)
Distribution – No./with data (%)			<0.001	
>12,000	152/2,854 (5.3)	160/1,117 (14.3)		312/3,971 (7.9)
<4,000	529/2,854 (18.5)	137/1,117 (12.3)		666/3,971 (16.8)
Neutrophil count				
Median (IQR) – cells/ µL	3,920 (2,800 – 5,560)	5,300 (3,530 – 7,700)	<0.001	4,200 (2,920 – 6,120)
<1,000 cells/ µL – No./with data (%)	51/2,848 (1.8)	24/1,113 (2.2)	0.448	75/3,961 (1.9)
Lymphocyte count				
Median (IQR) – cells/ µL	1,000 (700 – 1,360)	780 (540 – 1,160)	<0.001	900 (640 – 1,300)
<1,000 cells/ µL – No./with data (%)	1,423/2,852 (49.9)	727/1,111 (65.4)	<0.001	2,150/3,963 (54.2)
Neutrophil-to-lymphocyte ratio				
Median (IQR)	3.9 (2.5 – 6.5)	6.6 (3.7 – 11.4)	<0.001	4.5 (2.7 – 7.7)
Distribution – No./with data (%)				
Tertile 1	1,094/2,839 (38.5)	222/1,106 (20.1)	<0.001	1,316/3,945 (33.4)

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Tertile 2	1,005/2,839 (35.4)	309/1,106 (27.9)		1,314/3,945 (33.3)
Tertile 3	740/2,839 (26.1)	575/1,106 (52.0)		1,315/3,945 (33.3)
Platelets				
Median (IQR) – number x109/L	181,000 (143,000 – 229,000)	168,000 (130,000 – 221,000)	<0.001	178,000 (139,000 – 226,000)
Platelets < 150,000 – No./with data (%)	831/2,842 (29.2)	416/1,118 (37.2)	<0.001	1,247/3,960 (31.5)
Prolonged APTT (>39.2 seconds or ratio>1.25) – No./with data (%)	161/2,232 (7.2)	133/880 (15.1)	<0.001	294/3,112 (9.4)
INR				
Median (IQR)	1.1 (1.0 – 1.2)	1.2 (1.1 – 1.3)	<0.001	1.1 (1.0 – 1.2)
INR > 1.1 – No./with data (%)	954/2,376 (40.1)	549/925 (59.3)	<0.001	1,503/3,301 (45.5)
D-Dimer				
Median (IQR) – ng/mL	548 (328 – 934)	740 (410 – 1,590)	<0.001	580 (339 – 1,040)
High D-dimer levels (>500 ng/mL) – No./with data (%)	639/1,184 (54.0)	253/379 (66.7)	<0.001	892/1,563 (57.1)
Glucose				
Patients – No. with data	2,766	1,084		3,850
Median (IQR) – mg/dL	106 (93 – 126)	125 (104 – 165)	<0.001	110 (95 – 136)
Creatinine				
Patients – No. with data	2,832	1,111		3,943
Median (IQR)	0.88 (0.72 – 1.07)	1.10 (0.84 – 1.46)	<0.001	0.92 (0.74 – 1.18)
eGFR – mL/min/1.73 m^2 (CKD-EPI)				
Median (IQR)	84.1 (65.3 – 97.4)	60.2 (40.1 – 80.4)	<0.001	78.4 (56.5 – 93.6)
Distribution – No./with data (%)			<0.001	
>60	2,234/2,797 (79.9)	552/1,098 (50.3)		2,786/3,895 (71.5)
30 – 59	456/2,797 (16.3)	388/1,098 (35.3)		844/3,895 (21.7)

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<30	107/2,797 (3.8)	158/1,098 (14.4)		265/3,895 (6.8)
Sodium				
Patients – No. with data	2,825	1,109		3,934
Median (IQR) – mEq/L	138 (135 – 140)	137 (135 – 140)	0.008	138 (135 – 140)
Potassium				
Patients – No. with data	2,770	1,070		3,840
Median (IQR) – mEq/L	4.1 (3.8 – 4.4)	4.2 (3.8 – 4.6)	<0.001	4.1 (3.8 – 4.4)
ALT				
Median (IQR) – U/L	27 (18 – 42)	25 (17 – 38)	0.003	26 (18 – 41)
High serum levels ≥ 40 U/L and ≤200 U/L – No./with data (%)	630/2,369 (26.6)	190/870 (21.8)	0.021	820/3,239 (25.3)
High serum levels > 200 U/L – No./with data (%)	23/2,369 (1.0)	8/870 (0.9)		31/3,239 (1.0)
AST				
Median (IQR) – U/L	31 (23 – 45)	34 (23 – 52)	0.033	32 (23 – 48)
High serum levels ≥ 40 U/L and ≤200 U/L – No./with data (%)	680/2,051 (33.1)	291/750 (38.8)	0.011	971/2,801 (34.7)
High serum levels > 200 U/L – No./with data (%)	17/2,051 (0.8)	9/750 (1.2)		26/2,801 (0.9)
AST/ALT ratio – No./with data (%)			<0.001	
<1	675/2,013 (33.5)	166/733 (22.6)		841/2,746 (30.6)
≥1	1,338/2,013 (66.5)	567/733 (77.4)		1,905/2,746 (69.4)
Total Bilirubin				
Patients – No. with data	1,920	730		2,650
Median (IQR) – mg/dL	0.50 (0.37 – 0.71)	0.56 (0.39 – 0.87)	<0.001	0.50 (0.37 – 0.80)
Serum albumin				
Median (IQR) – g/dL	3.6 (3.2 – 4.0)	3.4 (3.0 – 3.8)	<0.001	3.5 (3.2 – 3.9)
Low albumin levels (< 3.4 g/dL) – No./with data (%)	310/991 (31.3)	198/420 (47.1)	<0.001	508/1,411 (36.0)

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Lactate dehydrogenase				
Median (IQR) – U/L	281 (215 – 382)	318 (250 – 463)	<0.001	290 (224 – 403)
High lactate dehydrogenase (>250) – No./with data (%)	1,154/1,895 (60.9)	510/683 (74.7)	<0.001	1,664/2,578 (64.5)
C reactive protein				
Median (IQR) – mg/L	44 (16 – 95)	87 (38 – 168)	<0.001	54 (20 – 116)
High C reactive protein levels (>5 mg/L) – No./with data (%)	2,388/2,654 (90.0)	990/1,023 (96.8)	<0.001	3,378/3,677 (91.9)
Procalcitonin				
Median (IQR) – ug/L	0.09 (0.05 – 0.16)	0.22 (0.10 – 0.56)	<0.001	0.11 (0.06 – 0.25)
High procalcitonin levels (>0.50 ug/L) – No./with data (%)	105/1,135 (9.2)	119/439 (27.1)	<0.001	224/1,574 (14.2)
Creatine kinase				
Median (IQR) – U/L	90 (56 – 169)	101 (56 – 217)	0.048	92 (56 – 182)
High creatine kinase levels (>190) – No./with data (%)	184/882 (20.9)	102/336 (30.4)	<0.001	286/1,218 (23.5)
Ferritin				
Median (IQR) – ug/L	611 (278 – 1,238)	792 (400 – 1,670)	0.002	649 (301 – 1,363)
High ferritin levels (>300 ug/L) – No./with data (%)	315/433 (72.7)	125/153 (81.7)	0.028	440/586 (75.1)
Interleukin-6				
Median (IQR) – pg/mL	33 (13 – 77)	117 (40 – 512)		42 (16 – 105)
High interleukin levels (>4.3 pg/mL) – No./with data (%)	175/201 (87.1)	58/58 (100.0)	0.004	233/259 (90.0)

Abbreviations: IQR, interquartile range; WBC, white blood cell count; eGFR, estimated glomerular filtration rate; CKD-EPI, chronic kidney disease epidemiology collaboration; APTT, activated partial thromboplastin time; INR, international normalized ratio; ALT, alanine, aminotransferase; AST, aspartate aminotransferase.

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Table 3. Independent predictors of death in the different clusters of variables

	HR (95% CI)	***P* value**
Sociodemographic characteristics		
Male sex	1.52 (1.33 – 1.73)	<0.001
Age (ref. 0-49 yrs.)		
50-65	3.76 (2.43 – 5.83)	<0.001
66-79	8.87 (5.85 – 13.43)	<0.001
80+	20.75 (13.72 – 31.37)	<0.001
Comorbidities		
Hypertension	1.81 (1.56 – 2.09)	<0.001
Chronic heart disease	1.58 (1.38 – 1.81)	<0.001
Diabetes	1.23 (1.07 – 1.41)	0.003
Chronic pulmonary disease (not asthma)	1.40 (1.21 – 1.61)	<0.001
Obesity	1.21 (1.01 – 1.44)	0.036
Chronic kidney disease stage 4 (eGFR < 30 mL/min/1.73m^2)	1.55 (1.26 – 1.91)	<0.001
Liver cirrhosis	1.59 (1.03 – 2.43)	0.034
Chronic neurological disorder	1.30 (1.08 – 1.57)	0.006
Cancer	1.59 (1.33 – 1.90)	<0.001
Dementia	2.28 (1.90 – 2.73)	<0.001
Admission signs and symptoms		
Headache	0.50 (0.37 – 0.68)	<0.001
Myalgia/Arthralgia	0.70 (0.59 – 0.84)	<0.001

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Anosmia	0.50 (0.22 – 1.14)	0.099
Cough	0.70 (0.60 – 0.80)	<0.001
Sputum production	1.26 (1.09 – 1.47)	0.002
Dyspnea	1.93 (1.69 – 2.19)	<0.001
Chest pain	0.64 (0.51 – 0.81)	<0.001
Vomiting/nausea	0.77 (0.62 – 0.95)	0.016
Altered consciousness	2.26 (1.93 – 2.66)	<0.001
Vital signs		
Low SaO_2 (age-adjusted)[a]	2.62 (2.29 – 3.00)	<0.001
Laboratory parameters		
WBC count (ref. <4,000 cells/x10^9/L)		
4,000-12,000	1.11 (0.91 – 1.35)	0.323
>12,000	1.54 (1.18 – 2.01)	0.002
Neutrophil count (ref. ≥1,000 cells/μL)		
<1,000	1.77 (1.12 – 2.79)	0.015
Neutrophil-to-lymphocyte ratio (ref. <3.22 [Tertile 1])		
3.22-6.33 [Tertile 2]	1.41 (1.17 – 1.69)	<0.001
>6.33 [Tertile 3]	2.38 (1.99 – 2.84)	<0.001
Platelets (ref. ≥150,000 x 10^9/L)		
<150,000	1.41 (1.24 – 1.60)	<0.001
Prolonged APTT (>39.2 seconds or ratio>1.25)	1.34 (1.09 – 1.64)	0.006
INR (ref. ≤1.1)		

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>1.1	1.49 (1.28 – 1.73)	<0.001
eGFR (ref. >60 mL/min/1.73m^2)		
30-59	2.24 (1.95 – 2.58)	<0.001
<30	2.68 (2.21 – 3.25)	<0.001
ALT (ref. <40 U/L)		
40-200	0.84 (0.71 – 0.99)	0.042
>200	0.86 (0.42 – 1.78)	0.692
C reactive protein (ref. ≤5 mg/L)		
>5 mg/L	2.43 (1.69 – 3.49)	<0.001

[a]Age-adjusted low SaO2 ≤90% for patients aged >50 years and ≤93% for patients aged ≤50 years

Abbreviations: SaO2, arterial oxygen saturation; WBC, white blood cell count; eGFR, estimated glomerular filtration rate; CKD-EPI, chronic kidney disease epidemiology collaboration; APTT, activated partial thromboplastin time; INR, international normalized ratio; ALT, alanine, aminotransferase.

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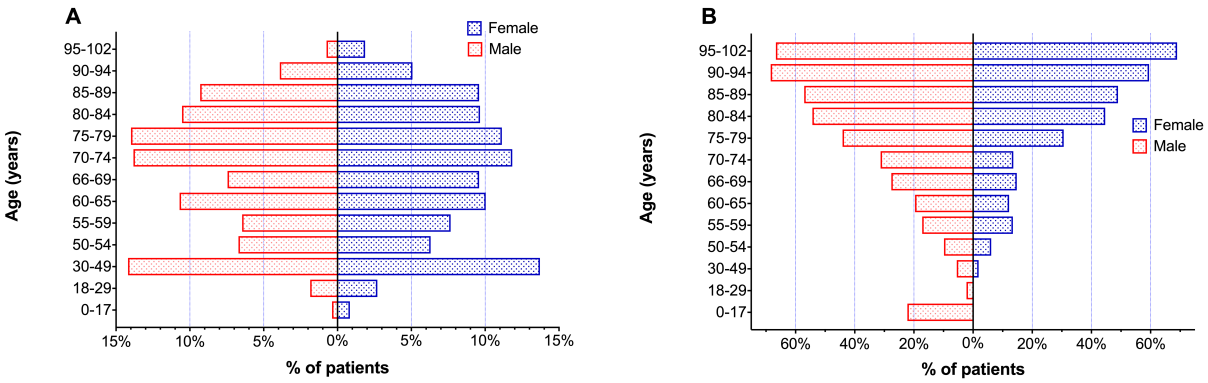

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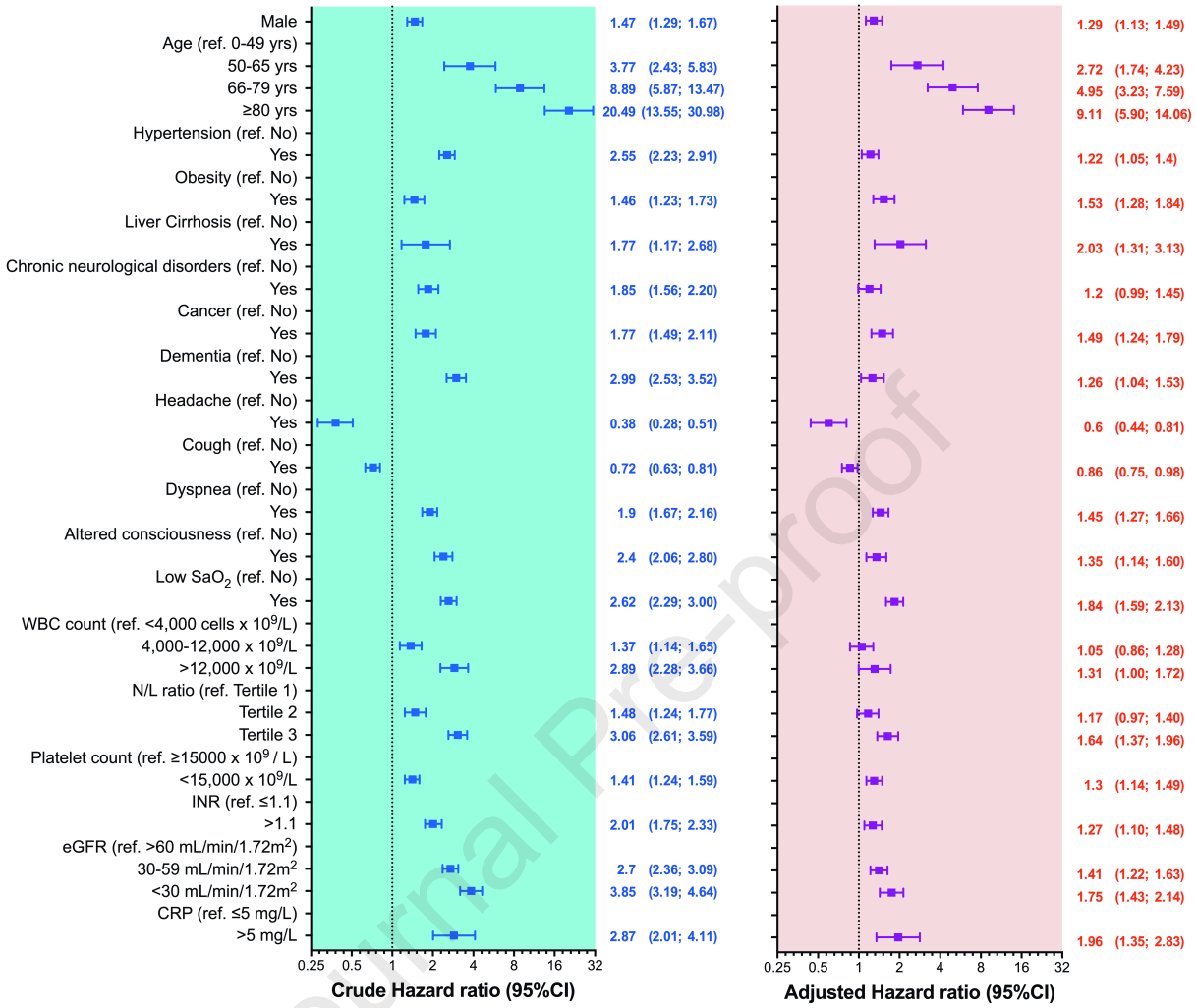

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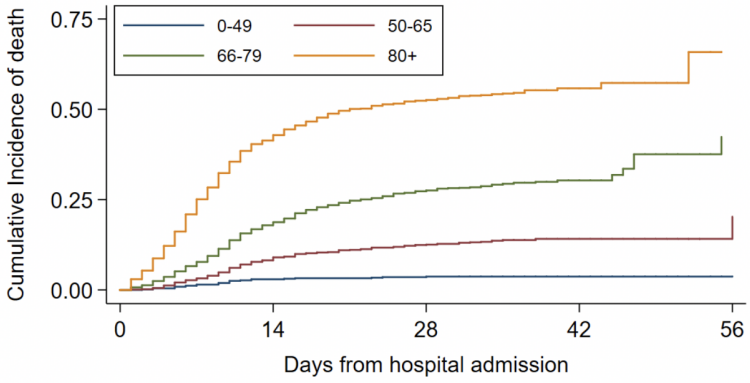
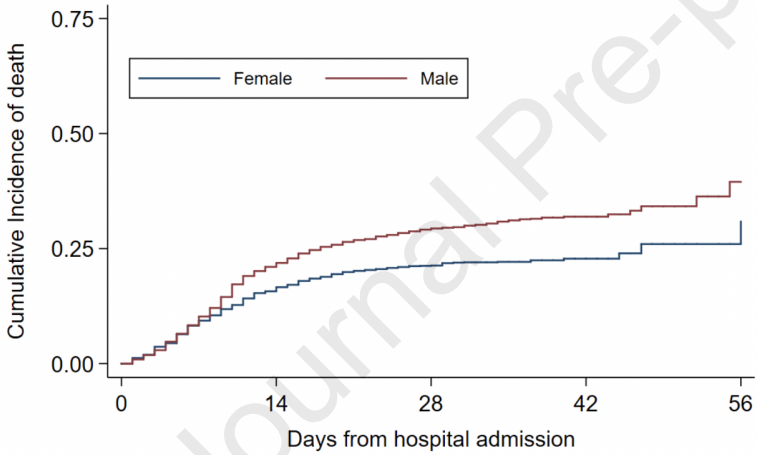


Number at risk

0-49	676	656	652	89	5
50-65	964	885	844	104	14
66-79	1380	1133	1003	99	12
80+	1008	591	480	49	2

B



Number at risk

Female	1553	1309	1223	124	15
Male	2431	1920	1723	213	18

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