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Early hydroxychloroquine is associated with an increase of survival in COVID-19 patients: an observational study.

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Summary: Hydroxychloroquine has shown in vitro activity against SARS-CoV-2. Here we present an observational study. We analysed data from 164 patients admitted to our hospital diagnosed with COVID-19. Hydroxychloroquine treatment was associated with an increase in the mean cumulative survival.

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ABSTRACT

Background: Although no specific treatment for COVID 19 has been proven effective yet, some drugs with in vitro potential against SARS-CoV-2 virus have been proposed for clinical use. Hydroxychloroquine has in vitro anti-viral and immunomodulatory activity, but there is no current clinical evidence of its effectiveness on the outcome of the disease.

Methods: We enrolled all 18-85 years old inpatients from Central Defense Hospital, Madrid, Spain, who were hospitalised due to COVID-19 and had a definitive outcome (either dead or discharged). We used a statistical survival analysis.

Results: We analysed 220 medical records. 166 patients met the inclusion criteria. 48,8 % of patients not treated with HCQ died, versus 22% in the group of hydroxychloroquine (p=0,002). According to clinical picture at admission, hydroxychloroquine increased the mean cumulative survival in all groups from 1,4 to 1,8 times. This difference was statistically significant in the mild group.

Conclusions: in a cohort of 166 patients between 18 to 85 years hospitalised with COVID-19, hydroxychloroquine treatment with an initial loading dose of 800mg improved patient survival when admitted in early stages of the disease. There was a non-statistically significant trend towards survival in all groups, which will need to be clarified in subsequent studies.

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FOOTNOTE PAGE

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-No funding sources were used in this study

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-This study has not been presented previously

Yours sincerely,

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INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by SARS-CoV-2, a recently discovered coronavirus in China. Until April 29th, 2020, the disease has spread over 213 countries, with almost 3 million infected people and more than 200.000 deaths (1). Despite being globally considered a mild infection in 80% of cases, moderate and severe cases can lead to death. At present, clinical management only includes supportive care, with supplementary oxygen and mechanical ventilation support when indicated. Several old and novel therapeutic approaches are being currently evaluated, since no specific treatment has been proven effective yet (2). Spain has been heavily affected by COVID-19, with more than 200.000 people infected and more than 24.000 deaths.

At the beginning of the pandemic, the Spanish Ministry of Health, supported by several working groups and scientific societies, formulated and implemented a clinical guideline for the management of COVID-19 in Spain. Several drugs were recommended for treatment (3): Lopinavir/Ritonavir (4,5,6), Remdesivir (4,7) (only for severe cases), Interferon alfa (8,9) and beta (10) and Tocilizumab (11,12). However, factors such as the fast expansion of the outbreak, with an increasing number of severe cases and deaths, along with stock problems and lack of definitive clinical evidence resulted in the emergence of various local hospital guidelines. Each set of guidelines was formulated on the basis of personal experience and a limited number of reported cases, while others were based on pathophysiological theories that haven´t been verified or proven correct yet. Glucocorticoids (13), azithromycin (14), and other immunomodulators have been used among some others.

After reviewing the guideline recommendations for treatment of COVID-19 published by the National Health Commission of the People's Republic of China (15), our institution decided to add the use of hydroxychloroquine to the stablished clinical protocol. Chloroquine

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(CQ), an aminoquinoline that has been used for prevention and treatment of malaria, has shown in vitro efficacy against SARS-CoV(16,17) therefore its effectiveness against COVID-19 was hypothesized. CQ can affect virus infection in many ways; the antiviral effect depends in part on the extent to which the virus utilizes endosomes for entry into the cell. Furthermore, HCQ has been found to be more potent than CQ to inhibit SARS-CoV-2 in vitro (18). However, there is no clinical evidence published in the current literature that supports the use of CQ/HCQ as treatment for COVID-19.

We conducted a systematic review of the literature using MEDLINE (covering January 1st, 2000 to April 3rd, 2020) using the following terms: (COVID-19 OR coronavirus OR sars-cov2) AND (hydroxychloroquine OR chloroquine). We excluded duplicated studies, those articles related to coronavirus infections in animals, and related to other diseases. The records have been classified by two independent reviewers (kappa=1). We selected 11 original studies (including 2 clinical trials), 11 reviews (1 systematic, 10 non-systematic) and 21 other publications (letters, case reports, news, consensus documents). There were only 2 original articles including patients with COVID-19 infection: 1 randomized clinical trial (19) including 10 patients (3 severe and 7 moderate cases) treated with CQ 500mg orally twice-daily for 10 days, and 12 patients (5 severe and 7 moderate cases) treated with Lopinavir/Ritonavir 400/100mg orally twice-daily for 10 days. The other article is a non-randomized clinical trial (14) including 26 patients receiving HCQ 200 mg, three times per day during ten days (6 of them with azithromycin) and 16 controls.

During the first days of the pandemic, HCQ was not considered in the local protocol. Afterwards, there were shortages in HCQ distribution. Due to these factors, two groups of patients were generated, those who received HCQ and those who didn't, both groups with similar characteristics. This situation gave us the opportunity to study the differences that arised

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between the two groups. Some other reasons for which some patients didn't receive HCQ were the potential side effects (arrythmias, drug interactions) or the patient's denial to give consent for an off label use of the drug.

While waiting for the results of larger clinical trials, that may confirm the association between endpoints and the definitive outcomes of patients, results from retrospective analysis from regular clinical practice may be useful. The main purpose of this study was to assess the mean cumulative survival in two different therapeutic regimens: with or without HCQ.

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METHODS

-Study design and participants: observational cohort study. We enrolled all adult inpatients from Central Defense Hospital "Gómez Ulla", Madrid, Spain, who were hospitalised for COVID-19 infection and had a definitive outcome (either dead or discharged). COVID-19 diagnosis was defined according to Spanish Ministry of Health definition from 31st March, 2020, including confirmed cases (PCR positive for any SARS-CoV-2 gene in respiratory samples - oropharyngeal swabs or sputum) and likely positive cases (bilateral interstitial pneumonia with clinical picture compatible with a COVID-19 diagnosis with no laboratory tests or non-concluding SARS-CoV-2 test). Discharge was considered, but it was analysed separately to either, discharge to home or to a "hotel-hospital" (temporary low-care medical facilities in Madrid hotels adapted for patients in the recovery phase, with no oxygen or intravenous requirements, who could be discharged from hospital but who had no possibility to properly complete the quarantine period at home).

The research protocol was approved by the Ethics Committee on Clinical Investigation of the Ministry of Defense of Spain. The requirement for informed consent was waived by the Ethics Committee. After a preliminary exploratory analysis of the outcomes of the first 220 patients, study was stopped, and the investigators considered mandatory a deep analysis and early publishing of the results due to the relevant differences on survival depending on the treatment used.

-Data collection: demographic, clinical, laboratory, treatment and outcome characteristics of the patients were extracted from the electronic medical records by two physicians. In case of differences in interpretation, a third investigator checked the medical records and clarified any difference. After collecting the data, the information was anonymized removing any reference to the patient's ID prior to the statistical analysis. The primary investigator and statistic analyser had no access to the medical records or patients ID.

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-Laboratory procedures: Methods for laboratory confirmation of SARS-CoV-2 infection have been described elsewhere (20). SARS-CoV-2 PCR test were performed in Clinical Microbiology Laboratory, Central Defense Hospital, Madrid.

Routine blood examinations included whole blood count, coagulation profile, serum biochemical tests (including renal and liver function, lactate dehydrogenase, and electrolytes). Interleukin-6 (IL-6), serum ferritin, myocardial enzymes and procalcitonin were recovered for several but not all patients. Furthermore all patients received chest X-ray. Frequency of examinations was determined by the treating physician.

-Definitions: severity of clinical picture at admission was defined according to Ministry of Health of Spain national treatment protocol, March 19th, 2020: mild (no hypoxemia, no respiratory insufficiency), moderate (hypoxemia and / or moderate respiratory insufficiency), severe (severe hypoxemia, severe respiratory distress, poor overall status). Hypertension was defined as previous arterial hypertension requiring any pharmacological treatment. Diabetes Mellitus was defined as previous hyperglycaemia requiring any pharmacological hypoglycaemic treatment. Dyslipidaemia was defined as previous alteration in lipid profile requiring pharmacological treatment. Cardiomyopathy was defined as any previous diagnosis of cardiac chronic disease or acute cardiac event. Respiratory disease was defined as any previous lower respiratory tract chronic disease requiring chronic pharmacological treatment. Cancer was defined as any previously diagnosed malignancy. Dementia was defined as any mental chronic disease altering cognitive capabilities. Lymphopenia was defined as less than 1000 lymphocites/ml. High LDH values were defined as those higher than 400 U/l. High CRP values were defined as those greater than 14 mg/dL. High D-dymer values were defined as those greater than 1000 ng/ml.

- HCQ/CQ selection and dose: Hospital treatment protocol selected hydroxychloroquine over chloroquine considering its improved *in vitro* activity profile (EC50=0.72 µM vs. EC50=5.47

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µM) (18). Despite Yao et al. manuscript's suggestions of a loading dose of 400 mg twice daily of hydroxychloroquine (18), we finally considered a loading dose of 800 mg + 400 mg, followed by a maintenance dose of 400 mg a day based on: 1) the hypothetical benefit of reaching the steady state and the EC90 as soon as possible in the case of this acute viral infection, 2) this is the regime accepted by the regulatory agency for acute malaria treatment, and therefore a safe and well-known dose by physicians. Nevertheless, some elderly patients didn't receive the extra loading dose of 800mg in order to avoid side effects and drug interactions.

-Other treatments: patients in both groups were treated with other drugs with potential activity against SARS-CoV-2 and/or COVID-19 immune disorders leading to ARDS. The list includes antivirals (lopinavir/ritonavir), immunomodulators (interferon beta), and/or anti-inflammatory drugs (steroids and/or tocilizumab)

-Statistical analysis: Quantitative variables were described with the arithmetic mean and its standard deviation and the median with its interquartile range. We used the absolute and relative frequency (%) for qualitative variables. The hypothesis tests used were the Chi2 Pearson or Fisher's exact test, the Student's T test or the Mann Whitney test, the one-way ANOVA, with the Bonferroni test for multiple comparisons, and Kruskal Wallis test. The survival analysis was performed using with the Kaplan Meier test and the comparison of factors was done with the Mantel Cox Log Rank test. A $p < 0.05$ was considered statistically significant. Logistic regression for multivariant analysis was performed with $p<0,250$ level as a screening criterion for selection of candidate variables. Statistical analysis was performed using the Windows software package SPSS (version 25).

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FINDINGS

We studied the first 220 “discharge” or “death” medical reports on COVID-19 wards, in Central Defense Hospital “Gómez Ulla”. We excluded 22 patients who were admitted to a COVID-19 ward but in the end didn’t have a confirmed clinical or microbiological diagnosis of COVID-19. 32 patients above the age of 85 years were excluded (during the first weeks of the pandemic, after evaluation of the risk-benefit balance, the Hospital's COVID-19 treatment concluded to not use off-label treatments for these patients) and 1 patient younger than 18 years (not attended by COVID-19 team). Ultimately, we included 166 patients in the study (figure 1). 83 patients had mild clinical picture at admission, 48 moderate and 35 severe. 118 Patients survived (90 were discharged of which 29 were discharged to “hotel-hospital”) and 48 died.

123 patients were treated with HCQ versus 43 patients who didn’t receive HCQ. 48,8 % of patients not treated with HCQ died versus 22% in the group of HCQ (p=0,002). Age distribution according to the severity at admission was homogeneous between HCQ and non-HCQ treatment groups when the clinical picture was mild (57,6 years HCQ – 58,4 years non-HCQ, p=0,865) or moderate (63,8 years HCQ – 70 years non-HCQ, p=0,269). Patients with severe clinical picture at admission treated with HCQ were younger than those who were not treated with HCQ (70,4 years HCQ -78,3 years non-HCQ, p=0,036) (table 1).

Comorbidities (table 2) were similar in both groups, except for cardiopathy (p=0,05) and dementia (p=0,022). Differences in treatment according to cardiopathy were expected because of the side effects of CQ/HCQ (prolongation of QT interval). Analytical data at admission was similar on both groups (table 2).

Mean hospital stay was 6 (5) days in the HCQ group and 5(7) days in the non-HCQ group (no significant difference, p=0,25).

Median (IQR) from the beginning of symptoms to the start of treatment with HCQ was 7(6) days. Mode was 7 days after symptoms onset. The median Md (IQR) of time elapsed from

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onset of symptoms to start of treatment was of 7 (7.25) days for the mild group, 7 (6.8) days for the moderate group and 5 (4) for the severe group, these differences being statistically significant (p = 0.01). Nervertheless, median (IQR) from hospital admission to the start of treatment with HCQ was 1(1) days, with no differences according to clinical picture at admission (p=0,223).

There was a clear increase in the accumulated survival rates in the 3 levels of clinical picture at admission favourable to the group treated with HCQ (table 3). In the mild group, their mean cumulative survival was increased 1.8 times in the group treated. In the moderate group the mean cumulative median survival was 1.4 times higher in the group treated. Finally, in the severe group the mean cumulative survival was 1.6 times greater in those treated.

In the mild group, the mean cumulative survival was 14.4 days (95% CI: 13.7-15.2 days) in those treated with HCQ and 8.2 days (95% CI: 6.5-9.9 days) in the untreated group, being this difference of 6.2 days statistically significant (p = 0.032).

In the moderate group, a trend towards longer survival was observed, but without reaching statistical significance. The mean cumulative survival was 10.9 days (95% CI: 9.3-12.5 days) in those treated with HCQ and 7.7 days (95% CI: 4.4-10.9 days). In the untreated group, this difference of 3.1 days was not statistically significant (p = 0.205).

In the severe group, the mean cumulative survival was 6 days (95% CI: 3.3-8.5 days) in those treated with HCQ and 4 days (95% CI: 1.7-6.1 days) in the untreated group. This difference of 2 days was not statistically significant (p = 0.297).

A multi-variant analysis or survival was performed, including comorbidities and analytical values at admission (table 4). The analysis excluded confusion bias on the increased survival in HCQ group: HCQ treatment was an independent predictor of lower mortality (p=0,003, 95% CI 0,012 – 0,402). Other independent predictors of survival were two comorbidities (cardiopathy, p=0,010, 95% CI 0,053-0,672, and dementia, p=0,013, 95% CI 0,002

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to 0,489), and two analytical conditions at admission: lymphopenia (p=0,026, 95% CI for lymphocites higher than 1.000/ml: 1,212-19,686).

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INTERPRETATION

From our known this is the first study showing an improvement of survival in a significant number of patients with a specific drug treatment for COVID-19. There was a clear increase in survival from 1,4 to 1,8 times to survival in those patients treated with HCQ. The cohort of patients with mild clinic at admission had clearly better outcomes when treated with HCQ.

These results were obtained in patients treated early (first week since symptoms onset, first day after admission). We theorise that the antiviral effect is only effective in early stages of the disease, before the immunomodulated ADRS development (21). This could explain the better outcomes of patients with mild symptoms being, treated with HCQ before the establishment of ADRS . Similarly, the different outcomes with other drugs with potential activity against SARS-CoV-2 as lopinavir/ritonavir which failed to show effect on mortality reduction with a mean of 14 days since symptoms onset (22). Regardless, our findings about HCQ, a low-cost and easily available drug with few side effects, makes HCQ/CQ a good choice to begin clinical trials in hospitalised patients, and to consider a more extended off-label use of the drug in early stages of the disease (taking into consideration all the legal and ethical considerations about this use).

Subgroups of patients with moderate and severe condition at admission showed a tendence to survival, but with no statistically significant differences in their outcomes. It's likely that, due to the physiopathology of COVID-19 (21), once the patient starts the "cytokine storm" phase, the antiviral effect it's less or not useful, and immunomodulation of HCQ it's not powerful enough to stop the progression of ADRS. In any case, this could be clarified with a larger sample size, which we will further study for future reports.

There were significant differences in age mean in the HCQ / non-HCQ groups of patients with severe disease at admission. This could be explained due to the higher number of comorbidities of elder patients with severe condition at admission, which may have led clinicians

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to limit the therapeutic effort in some of them. Nevertheless, this should be studied deeper in further studies.

Overall, patients with dementia were less treated with HCQ. This could be explained because of potential drug interactions, which could have influenced their clinicians to not treat such patients with off-label, potentially dangerous drugs. Another reason could be the difficulty of administering oral drugs to those patients, some of them with difficulty swallowing, while not allowed to be accompanied by their relatives during isolation. This data that should be clarified in further studies since dementia was an independent predictor of mortality in the multi-variant analysis.

Analytical data showed a numeric, non-statistically significant, difference in D-dymer levels between the two groups: 558(716) HCQ group vs 1511(4570,5) non-HCQ group. During the first weeks of the pandemic D-dymer analysis was not performed to all patients at admission, therefore 120 (46,9%) patients didn't have this value recorded. This makes difficult to interpret this data. Nevertheless, D-dymer level at admission was not proven to be an independent predictor of mortality in the multi-variant analysis.

A unexpected data was found when the days from symptoms onset to hospital admission were analyzed. The mean days were fewer in those patients admitted with severe condition. This could suggest that there are subgroups with a higher risk of quick development of ADRS. Identifying their characteristics would be a key point to understand why the course of COVID-19 course is mild in most patients but severe, devastating and life-threatening in others. To the actual date, no substantial differences have been identified that could explain the different clinical courses of the disease.

Conclusion: In a cohort of 166 patients, age range 18 to 85, hospitalised with COVID-19, hydroxychloroquine treatment with an initial loading dose of 800mg increased the mean survival

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rate by 1.4 to 1.8 times. The increase was adjusted to the initial severity. This difference was statistically significant when the clinical picture at admission was mild.

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***Table 1**. General characteristics of the patients in both treatment groups (with and without HCQ)*

		HCQ Yes n=123	No n=43	p
Age (years) $\bar{x}(DE)$	Clinical picture at admission	61,5(16,2)	68,7(18,8)	0,012*
	Mild	57,6(15,7)	58,4(17,8)	0,865*
Age (years) $\bar{x}(DE)$	Moderate	63,8(16,5)	70(13,2)	0,269*
	Severe	70,4(13,4)	78,3(7,2)	0,036*
Sex n(%)	Male	76(61,8)	27(62,8)	0,907**
	Female	47(38,2)	16(37,2)	
	Death	27(22)	21(48,8)	
Final outcome n(%)	"Hospital Hotel"	26(21,1)	3(7)	0,002**
	Home	70(56,9)	19(44,2)	

*t Student; **χ2 Pearson

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***Table 2**. Clinical Comorbidities and Analytical Parameters of Patients on Admission in Both Treatment Groups.*

		HCQ Yes n=123 n(%)	No n=43 n(%)	p
Hypertension	Yes	49(69)	22(31)	0,214*
	No	74(77,9)	21(21,1)	
Diabetes	Yes	19(65,5)	10(34,5)	0,246*
	No	104(75,9)	33(24,1)	
Dyslipidaemia	Yes	39(68,4)	18(31,6)	0,190*
	No	84(77,8)	24(22,2)	
Cardiopathy	Yes	23(62,2)	14(37,8)	0,050*
	No	100(78,1)	28(21,9)	
Cancer	Yes	15(65,2)	8(34,8)	0,268*
	No	108(76,1)	34(23,9)	
Dementia	Yes	6(46,2)	7(53,8)	0,022**
	No	117(77)	35(23)	
Pulmonary disease	Yes	15(62,5)	9(37,5)	0,143*
	No	108(76,6)	33(23,4)	
Leukocytes µl		6320(3395)	8004(4530)	0,696***
Lymphocytes µl		1160(545)	860(730)	0,997***
LDH U/l		328(141)	296(216)	0,971***
GOT U/l		36(24)	28,5(37)	0,923***
PCR mg/dl		6,2(10,7)	12,1(16,8)	0,845***
PCT ng/ml		0,13(0,29)	0,59(4,38)	0,730***
Ferritin ng/ml		375(827)	321,5(1158)	0,144***
D dimer ng/ml		558(716)	1511(4570,5)	0,168***

**Chi2 Pearson; **Exact Fisher test; ***Mann Whitney test*

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***Table 3**. Increase of survival with HCQ according to clinical picture at admission (days)*

	Total	HCQ group	Non-HCQ group
Mild	14(IC95%:13-14,8)	14,4(IC95%:13,7-15,2)	8,2(IC95%:6,5-9,9)
Moderate	10,3(IC95%: 8,7-11,9)	10,9(IC95%:9,3-12,5)	7,7(IC95%:4,4-11)
Severe	5,2(IC95%:3,4-7,1)	5,9(IC95%:3,3-8,5)	3,9(IC95%:1,7-6,1)

*Log Rank (mantel Cox)

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***Table 4**. Significant outcomes of the multi-variant analysis of survival*

		B	Standard error	Wald	gl	Sig.	Exp(B)	95% C.I. for EXP(B) Lower	Higher
	Cardiopathy	-1,671	,650	6,609	1	,010	,188	,053	,672
	Dementia	-3,426	1,384	6,132	1	,013	,033	,002	,489
	Lymphopenia	1,586	,711	4,973	1	,026	4,884	1,212	19,686
	High RCP values	-1,413	,645	4,803	1	,028	,243	,069	,861
	HCQ treatment	-2,654	,889	8,914	1	,003	,070	,012	,402

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Figure 1. Patient inclusion flow chart

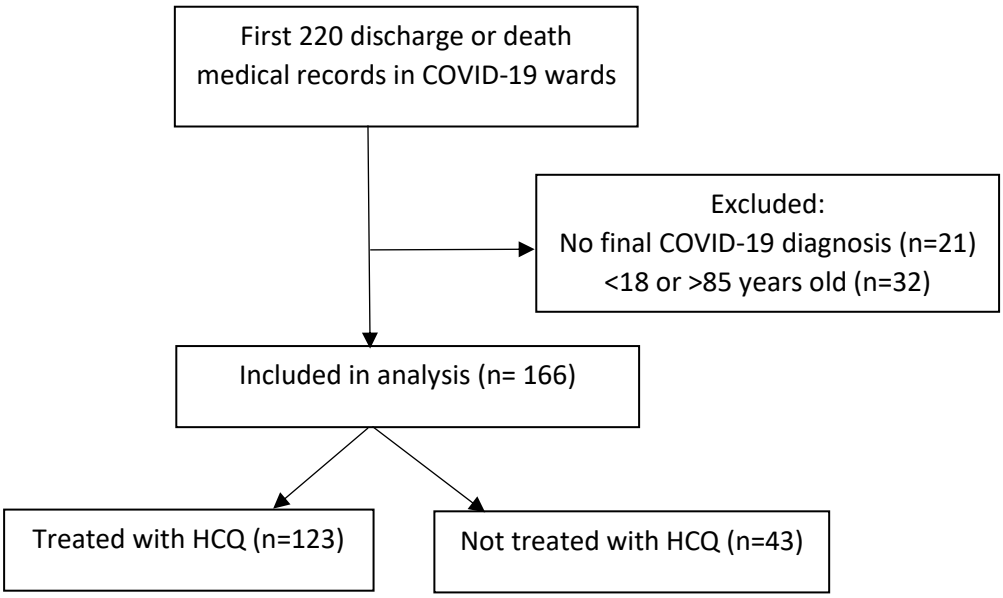

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Figure 2. Age distribution, according to severity at admission

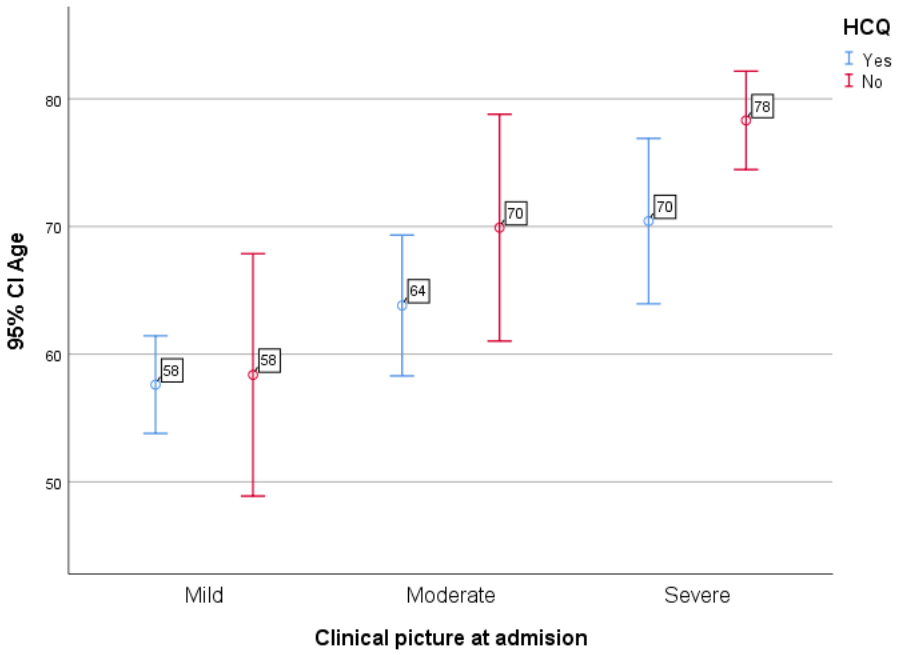

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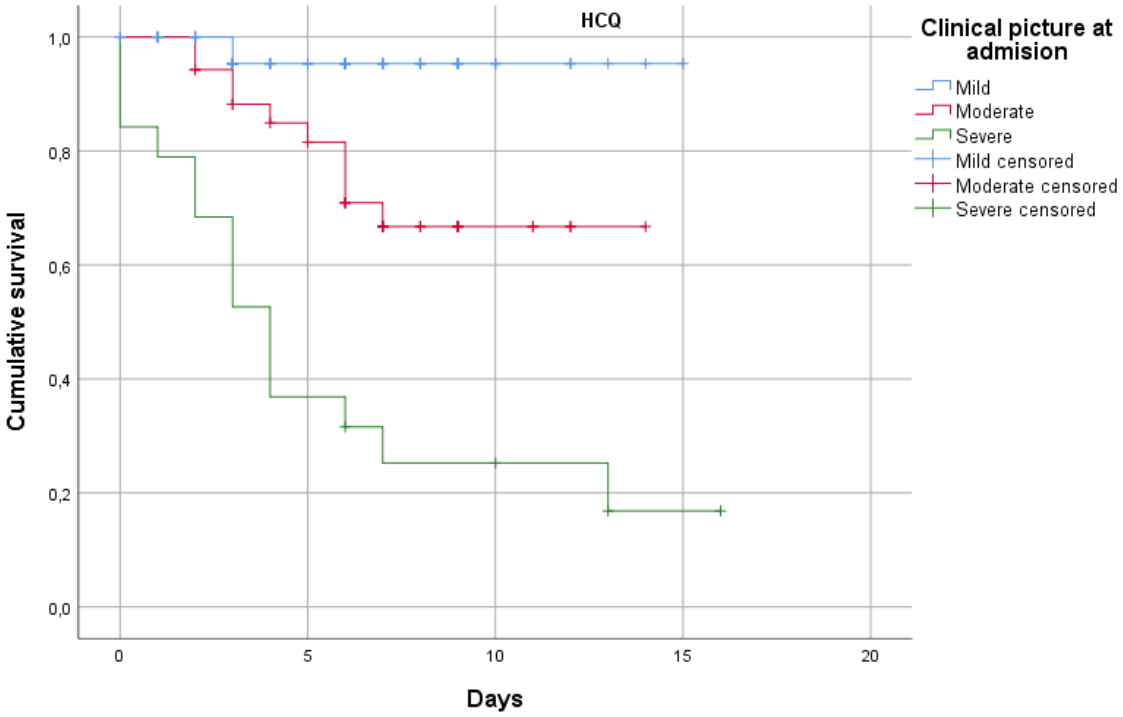
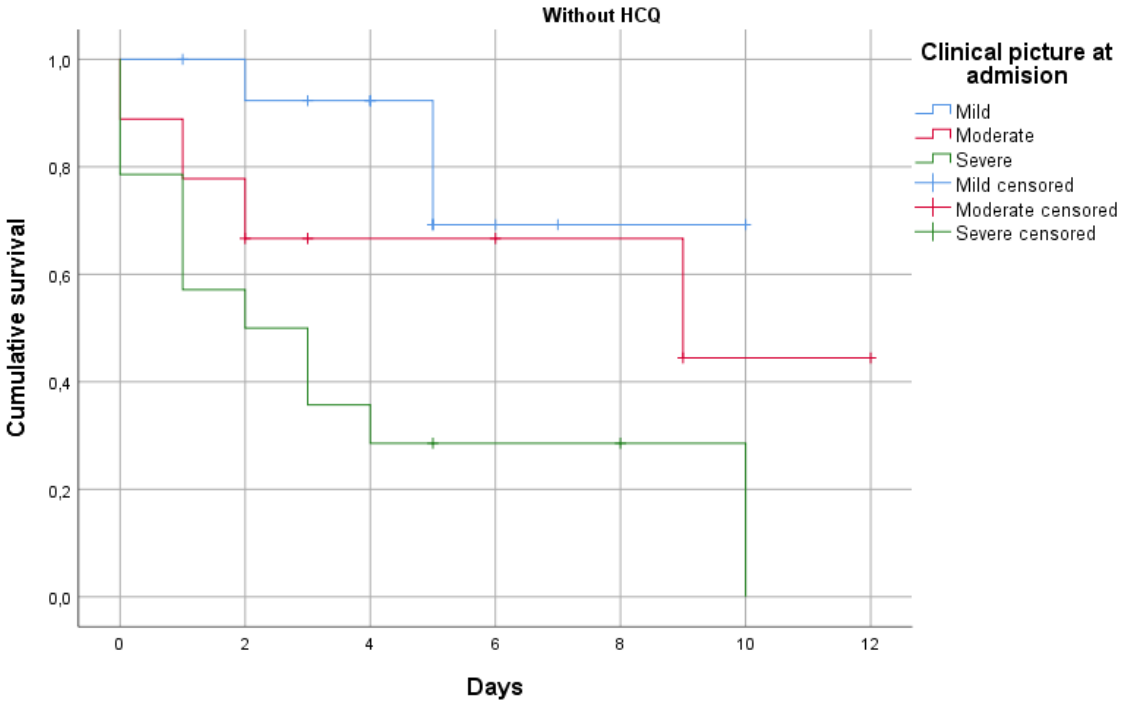
Figure 3. Kaplan-Meier Survival functions with/without HCQ

With HCQ



Without HCQ



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ANNEX 1. MEMBERS OF THE COVID 19 CENTRAL DEFENSE HOSPITAL "GÓMEZ ULLA" TEAM

Allergy Department:

Regina María Paulaskas Vasati, Enrique Gabriel Gómez González.

Anaesthesiology Department:

Pelet Pascual, Elvira. García Aroca, Miguel Ángel. Cantalejo Pérez, Francisco. Gago Sánchez, Alberto José. Rodríguez Martín, Ana. Rodríguez Sánchez, Dolores. Tejeda Fernández, Jose Luis. Santos, Elisabeth. Almagro Vidal, Inés. Álvarez Fdez., Lucía. Arranz Pérez, Rodrigo. Cabrera Serrano, Gemma. Fernández Peña, Alberto. González Del Pozo, Irene. Martín Oropesa, Raquel. Monteserín Matesanz, Cristina. Navarro Echevarría, Patricia. Olivera Moreno, Daniel. Vullo, Paula Agostina.

Cardiology Department:

Salvador Álvarez Antón, David Martí, Concepción Fernández Pascual, María José Morales, Andrea Rueda Linares, Carmen de Juan Bitria, Alexander Félix Marschall, Fredy Andrés Delgado Calva, Maria Belen Biscotti Rodil, Ricardo Concepción Suárez, Dámaris Caballeira Puentes.

CBRN and Infectious Diseases Unit

Lucía Elena Ballester Orcal, Francisco Javier Membrillo de Novales, Yolanda Martínez Martínez, Antonio Fe Marqués.

Clinical Microbiology Department:

María Mateo Maestre, María del Carmen Ybarra de Villavicencio, María Simón Sacristán, Maria Isabel Zamora Cintas, Almudena Rodriguez Aranda, Amelia Montserrat Carmona de Cózar, Maria Encarnación Mérida Arias, Jose Luis Martin Prieto.

Dermatology Department

Leire Sanchez Los Arcos, Cristina Collantes Rodríguez.

Digestive Medicine Department:

Asunción Ramos Meca, Elena Portales, Marian Ángeles García Mayor, Inmaculada Pérez Amarilla, Mar Rodríguez, Enrique de la Fuente, Gema Arranz, María Jesús Callejo, Natalia Zuberoa Rosado Dawid, Sandra María Caro López, Ana Isabel Sáez Sáez, María Domínguez Rodríguez.

Emergency Department:

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Jaime Rossiñol Ruiz, David Coca Benito, M. Luz Cano Izquierdo, M. Lourdes Rojas Bueno, M. Carmen Reche Caballero, Claudio Escobar Bargueño, Silvia Jiménez Zamora, Alfonso López Chollet, Marta Del Nido Alonso, Margarita Del Moral González, Miguel Muro Fernández, Marta Martín Vallejo, Elena Planchuelo Medina, Gabriel González Salazar, Fátima Ibáñez Estéllez, Rolando Sordo Díaz, Noelia Arroyo Pardo, Enrique Portela Filgueira, Ana María Martínez Molina, Beatriz Rato Barrio, Ignazio Taronna Latorre, Jessica D. Peña Vásquez, M. Eugenia Zornoza Pérez, María José Noguera Marín, Capitán Antonio Eloy Seva Delgado, Teniente Darlin M. Guzmán Rosario, Teniente Fabián Manjarrés Henríquez, Teniente Alvaro Rodríguez Rodríguez, Ana Betegón Sanz, Miguel Almazor Iribarren, M. Asunción Sánchez Gil, Juan Carlos Sánchez Sánchez-Gil, Dionisio Alastuey Martínez, Gonzalo Infante Pino, Eduardo De Vicente Cano, Estefanía Ruiz Alcaide, Andrea Matas Escamilla

Endocrinology Service:

Elena Mendoza, Teresa de Grado, Carmen Gil.

General and Digestive Surgery Department:

Oscar Marqueta García, Mariano Javaloyes Rodrigo, Miguel Ángel Sierra Ortega, Tcol Maria Isabel Sanchez-Seco Peña, Ignacio García Marirrodriga, Francisco Sanchez del Valle, Jose Antonio Sáez Montoro, Fernando Fernández Bueno, Yusef Mohamed Al Lal, Cristina López Muñoz, Patricia Tejedor Togores, Guillermo Fernández Díaz, Silvia Maestro Prieto. Luis de Nicolás Navas, Juan José Perez Alegre, Pablo Hernández Sanz.

Intensive Care Department:

Jorge Medina Segovia, Paloma Sanchez Mata, Rosario Fernandez Suero, Felix Maimir Jané, Luis Vicente Saenz Casco, Pilar Borrego Jimenez, Francisco Gijón Gallego, Esperanza Molero Silvero, Cesar Eugenio Gaona Coscia, Javier Sainz Cabrajas.

Infectious Diseases Unit

Germán Ramírez-Olivencia, Miriam Estébanez Muñoz, Begoña de Dios García, María Dolores Herrero Mendoza, Tatiana Mata Forte.

Internal Medicine Department:

María Jesús Sánchez Carrillo, María Navarro Téllez, Belén Esteban Lazareno, Raúl Ruiz Esteban, Javier Rodeles Melero, José María Rodríguez Fernández, María Eugenia Segovia, Elsa Labrada, Ana López Aparicio, Alejandro Estrada, Emma de Pablo, Álvaro Conesa, Ainhoa Gutiérrez, Irene Ruiz, Ana Roel, Xavier Álvarez Granda, Luisa Jimenez Reyes, Laura Checa, Lidia Romero, Paloma Lucena Calvet, Pedro Priego de Montiano, Francisco de Asís Fernández Riestra, Maria Antonia Menendez, Carmen González, Jose Ramón Toral Revuelta, Alba Ibáñez Botella.

Neurology Department:

Manuel Domínguez Salgado, Francisco Valenzuela, María del Rosario Antón Abarca.

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Oncology Department:

Carmen Arlanzón.

Paediatrics Department:

Carlota García, Noelia Valero Flores, Andrés Fernández Flores, María García Baró, Paula Polanco Zea, María José Hernández, Helena Viana Llamas.

Pharmacology Department:

María Henar Gonzalo Salado, Francisco Javier Sanchez Jimenez, Francisco José López Honduvilla, Paloma Sánchez López, Pilar Prats Oliván, María Jesús Méndez Fernandez, Laura Pedraza Nieto, Ana Acuña Vega, Andrea Correa Pérez, Paula Granda Lobato.

Pneumology Department:

Francisco Ramón Villegas Fernández, Andrés Rodero Baño, Gabriel J Caballero Rodriguez, Begoña de Juan Rodrigo, Sergio Campos Tellez, María Jesús Chillón, Alberto González Estebanez, Jose Javier Jareño Esteban, Carolin Wagner Struwing, María Castro Otero, Ana Ochoa Ruiz, Salvador de la Torre Carazo, Ángela Hidalgo Herranz, Marta Perez Gallan, Diogenes José Alfonzo Martinez, Soledad Torres Tienza, Silvia Sans Perez, Cristina Yanlli Bonduki, Juan de Mesa, Carmen Lorenzo.

Preventive Medicine Department:

María Vicenta García Rosado, Ana Isabel López Figueras, Pilar Segura Cebollada, María Teresa Ledo Varela.

Psychiatry Department:

Marta Presa García, Victoria Juarez Calvo, Catalina Iglesias García, Cristina Rodriguez Villarino, Daniel Fernández Faber, Maria Plaza Yuste, Celia María Hernández Caro, Jose David Cozar Ortiz, Coral Esperanza Torrente, Cristina Rodriguez Delgado.

Rehabilitation Department:

Carlos Mora Jordá, Rebeca Maruenda Fernández, Ana Tovar Cifuentes, Guillermo Fernández García Ruiz-Calero, María De los Ángeles Rodríguez Gamero, Cristina Novo Navarro, Maria Victoria Lorenzo Suberviola.

Rheumatology Department:

María Ahijón, Raul Veiga.

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Traumatology Department

Javier Areta Jiménez, Jose Luis Bernacer López, Roberto Trapote Sanmartín, Jose Luis Sopesen Veramendi, Marcos Fernandez Gayol, Jose Adolfo Orellana Gomez-Rico, Francisco González Prieto, Ana Arrollo Perez, Montserrat Martinez Roldan, Diana Crego Vita, Carlos Rodríguez Moro, Arturo Muñoz Ruiz, Rafael García Cañas, Raquel Vallez Romero, Ricardo Vethencourt Koifman, Gonzalo Hernandez Fernandez, Ricardo Baños Turza, Irene Portellano Pascual, Nelson Lasluisa Molina, Monica Huecas Martinez, Alberto Granado Llamas, Azucena Martín Herreros, Alfonso Rodriguez Mejías, Serafín Mihanda Eliquya, Felipe Velasco Vaquero, María Prieto Vazquez.