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ORIGINAL ARTICLE

Impact of renal function on admission in COVID-19 patients: an analysis of the international HOPE COVID-19 (Health Outcome Predictive Evaluation for COVID 19) Registry

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Abstract

Background Coronavirus disease 2019 (COVID-19) is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite its international aggressive extension, with a significant morbidity and mortality, the impact of renal function on its prognosis is uncertain.

Methods Analysis from the international HOPE-Registry (NCT04334291). The objective was to evaluate the association between kidney failure severity on admission with the mortality of patients with SARS-CoV-2 infection. Patients were categorized in 3 groups according to the estimated glomerular filtration rate on admission (eGFR > 60 mL/min/1.73 m^2, eGFR 30–60 mL/min/1.73 m^2 and eGFR < 30 mL/min/1.73 m^2).

Results 758 patients were included: mean age was 66 ± 18 years, and 58.6% of patient were male. Only 8.5% of patients had a history of chronic kidney disease (CKD); however, 30% of patients had kidney dysfunction upon admission (eGFR < 60 mL/min/1.73 m^2). These patients received less frequently pharmacological treatment with hydroxychloroquine or antivirals and had a greater number of complications such as sepsis (11.9% vs 26.4% vs 40.8%, p < 0.001) and respiratory failure (35.4% vs 72.2% vs 62.0%, p < 0.001) as well as a higher in-hospital mortality rate (eGFR > 60 vs eGFR 30-60 vs and eGFR < 30, 18.4% vs 56.5% vs 65.5%, p < 0.001). In multivariate analysis: age, hypertension, renal function, 0^2 saturation < 92% and lactate dehydrogenase elevation on admission independently predicted all-cause mortality.

Conclusions Renal failure on admission in patients with SARS-CoV-2 infection is frequent and is associated with a greater number of complications and in-hospital mortality. Our data comes from a multicenter registry and therefore does not allow to have a precise mortality risk assessment. More studies are needed to confirm these findings.

Keywords COVID-19 · Mortality · Registry · Prognosis · Acute kidney injury · Chronic kidney failure

Abbreviations

ACE2	Angiotensin-converting enzyme 2
AKI	Acute kidney injury
CKD	Chronic kidney disease
COVID-19	Coronavirus disease 2019
eGFR	Estimated glomerular filtration rate
RAAS	Renin–angiotensin–aldosterone system
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SIRS	Systemic inflammatory response syndrome

HOPE COVID-19 Investigators, Scientific Committee and collaborators are listed in Supplementary appendix.

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Introduction

In January, 2020, a novel virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified as the causative agent for a cluster of pneumonia cases initially detected in Wuhan City, Hubei province, China [1]. SARS-CoV-2, which causes the disease now named coronavirus disease 2019 (COVID-19), have spread from China to the rest of the world [2, 3].

Currently the percentage of asymptomatic infected carriers is unknown, but different studies indicate that this percentage could be very high [4]. In symptomatic patients, the clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death [5]. Among patients with confirmed SARS-CoV-2 infection, we encountered a significant number of patients with acute renal dysfunction. Some even progressed to renal failure and required dialysis. One of the main complications that are being observed in these patients is the rapid clinical deterioration that some people exhibit. In this sense, early estimation of risk factors for severe disease and death in these patients seems to be a priority. In previous reports of SARS and MERS-CoV infections, acute kidney injury (AKI) developed in 5–15% cases and carried a high (60–90%) mortality [6]. Nevertheless, the incidence and prognosis of acute kidney failure in SARS-CoV-2 patients is unknown and information about the clinical impact remains sparse.

Here, we present details of an international registry of patients discharged from a hospital with laboratory-confirmed or high suspicion SARS-CoV-2 infection and definite clinical outcomes. The clinical effects of renal function in SARS-CoV-2 infection were explored.

Methods

Study design and population

Renal function was recorded on admission from a cohort study of 758 patients with confirmed or highly suspected COVID-19 infection included in the multicenter international HOPE Registry (https://www.hopeprojectmd.com), Registry NCT04334291 on ClinicalTrials.gov. The HOPE-Registry was established through an international consortium. Detailed information about participating countries and hospitals, protocol and definitions are reported on website of the Registry. In this interim analysis hospital data and patients were included until the second of April 2020. All Patients discharged (deceased or alive) from any hospital center with a confirmed diagnosis or a COVID-19 high suspicion were included in the HOPE Registry. The local ethics committee approved this study and was consistent with the guidelines of Helsinki. A list of participating hospitals, investigators, collaborators and the protocol are available in the appendix.

Outcome definition

We assessed the impact of kidney failure severity on admission on the prognosis of 758 patients with COVID-19. Patients were stratified into three groups according to the estimated glomerular filtration rate (eGFR) on admission: Absence of significant renal failure if GFR > 60 mL/min/1.73 m^2; moderate renal failure if GFR between 30–60 mL/min/1.73 m^2; and severe renal failure if GFR < 30 mL/min/1.73 m^2. Creatinine clearance has been calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

Primary endpoint was defined as all-cause in-hospital death. Secondary outcomes were in-hospital complications such respiratory insufficiency, AKI, pneumonia, sepsis and embolic events. Chronic kidney disease (CKD) was identified based on the patient's medical history. AKI was identified at admission when the patient had no previous CKD and creatinine clearance at admission was < 60 mL/min/1.73 m^2. AKI during admission was diagnosed according the standard definition of AKI in adults: an increase in serum creatinine by ≥ 26 µmol/L (0.3 mg/dL) within 48 h, or an increase in serum creatinine to > 1.5 times baseline within the previous 7 days, or urine volume < 0.5 mL/kg/h for > 6 h. Respiratory insufficiency was defined by an arterial oxygen tension < 60 mmHg, and/or arterial carbon dioxide tension > 45 mmHg or both, or the presence of O2 saturation less than 92%, at room air.

Management and treatment

There is little direct evidence to inform management of COVID-19. Pending the publication of ongoing clinical trials, recently, the American Thoracic Society-led International Task Force has published some recommendations in which the important lack of evidence in this regard can be verified [7]. For this reason, the treatment used by each of the centers involved in this registry may differ, and it is based on individualized protocols according to their self-experience treating COVID-19 infection and their local hospital resources.

Statistical analysis

Data is presented as mean ± standard deviation for continuous variables with a normal distribution, median

(interquartile range) for continuous variables with a non-normal distribution, and as frequency (%) for categorical variables. Student's *t* test and the Mann–Whitney U-test were used to compare continuous variables with normal and non-normal distributions, when needed. The Chi squared-test or Fisher's exact test was used to compare categorical variables. Univariate analysis was performed for qualitative variables and reported as odds ratios (OR) with 95% CI. Given the multiplicity of variables, only factors with $p < 0.01$ on univariate analysis (dislipemia, diabetes mellitus, smoke, chronic kidney failure, heart disease, lung disease, cerebrovascular disease, connective disease, cancer, immunosuppression condition, RAAS-inhibitors treatment, aspirin treatment, anticoagulation treatment, statin treatment, saturation O2 < 92% on admission, d-dimer elevation, PCR elevation, lactate dehydrogenase elevation, eGFR on admission) were entered into the Cox multivariate regression analysis to define independent risk factors for the main outcome. Possible collinearity and interactions were evaluated with the introduction of multiplicative terms calculating the tolerance and the variance inflation factor. The relationship between creatinine clearance and the predicted probability of death was graphically represented after modeling this association using fractional polynomials. All tests were two-sided, and a P value less than 0.05 was considered statistically significant. Statistical analysis was performed with the IBM SPSS 20.0 software package and STATA software, version 15.

Results

Baseline characteristics

A total of 758 patients were included in our study. The percentage of testing positive patients for SARS-CoV2 infection by Nasopharyngeal PCR was 90.8%. Table 1 shows the baseline characteristics of COVID-19 patients. Mean age was 66 ± 18 years, 58.6% of patient were male and the median duration from illness onset to admission was 6 (IQR 5) days. Of the total reported patients 317 (48.9%) had hypertension, 290 (38.7%) dyslipidemia, 138 (21.9%) diabetes mellitus, 149 (19.5%) and 199 (26.1%) had some previous pulmonary or cardiac condition, respectively. Only 8.5% of patients had a history of CKD, however, close 30% of patients had any sort of impaired kidney function according to their eGFR upon hospital admission.

Patients were categorized in 3 groups according to eGFR on the admission (eGFR > 60 mL/min/1.73 m^2 [n = 526], eGFR 30–60 mL/min/1.73 m^2 [n = 177] and eGFR < 30 mL/min/1.73 m^2 [n = 55]). When we compared these groups (Table 1), we observed that patients with renal injury (eGFR 30–60 mL/min/1.73 m^2 and eGFR < 30 mL/min/1.73 m^2 groups vs eGFR > 60 mL/min/1.73 m^2 group) were older and presented a greater number of comorbidities. Furthermore, these groups had more frequently received prior treatment with antiplatelets, anticoagulants and renin–angiotensin–aldosterone system (RAAS) inhibitors. Groups with poorer eGFR on admission had a higher proportion of CKD.

Comparison of clinical aspects on admission between different groups

Table 1 shows the comparison of signs, symptoms and laboratory test on admission between three groups. In general, patients with poorer kidney function (eGFR 30–60 mL/min/1.73 m^2 and eGFR < 30 mL/min/1.73 m^2 groups vs eGFR > 60 mL/min/1.73 m^2 group) went to the hospital sooner after the symptoms onset and they were in a worse clinical situation. Fever was the most frequent reason for seeking medical attention. We observed that groups with poorer renal function (eGFR 30–60 mL/min/1.73 m^2 and eGFR < 30 mL/min/1.73 m^2 groups) had a lower incidence of general symptoms (cough, anosmia, dysgeusia, myalgia or arthralgia); albeit, respiratory failure was more frequent. Laboratory parameters on admission suggestive of systemic inflammatory response (SIRS) or coagulopathies, such as D-dimer or lymphopenia, were also more frequent in patients with worse eGFR (eGFR 30–60 mL/min/1.73 m^2 and eGFR < 30 mL/min/1.73 m^2 groups).

Treatment and outcomes during admission

Management is depicted in Table 1. The specific drug most frequently used was hydroxychloroquine (79.7%), followed by antibiotics (70.7%) and antiviral drug, (lopinavir/ritonavir) (68.7%). Corticoids were prescribed in approximately 20% of the cases. Treatment with RAAS inhibitors was maintained in 14% of patients during admission. In the respiratory support sphere, prone was used in 10%, and non-invasive mechanical ventilation in 18%. An invasive mechanical ventilation approach was required in more than 5%. When we compared these groups according to eGFR, groups with poorer renal function on admission were less frequently treated with hydroxychloroquine (eGFR > 60 vs eGFR 30–60 vs and eGFR < 30, 82.3% vs 76.5% vs 63.5%, $p < 0.001$) and antivirals (Lopinavir/Ritonavir) (eGFR > 60 vs eGFR 30–60 vs and eGFR < 30, 71.3% vs 63.9% vs 58.0%, $p < 0.001$).

Regarding in-hospital events, the most common was bilateral pneumonia, reported in more than 75% of the cases, with associated respiratory insufficiency in 43.4%. Renal failure and sepsis or SIRS were common, in more than 15%. Sepsis and respiratory failure were more frequent in groups with eGFR < 60 ml/min/m^2 on admission. The incidence of AKI at or during admission in our series was 19.7%. When we analyze the development of AKI during admission, we

Table 1 Baseline characteristics, signs, symptoms, laboratory test, treatments, complications and outcomes of different groups according to the glomerular filtration rate

	eGFR > 60 mL/min/1.73 m^2 (N = 526)	eGFR 30–60 mL/min/1.73 m^2 (N = 177)	eGFR < 30 mL/min/1.73 m^2 (N = 55)	p
Female (%)	219 (41.6%)	68 (38.4%)	26 (47.3%)	0.487
Age (years)	61 ± 17	78 ± 11	79 ± 13	< 0.001
Hypertension	192 (36.6%)	132 (75.4%)	44 (80.0%)	< 0.001
Dyslipidemia	164(31.7%)	99 (57.6%)	25 (45.5%)	< 0.001
Diabetes	74 (14.6%)	42 (25.0%)	20 (37.7%)	< 0.001
Smoker	96 (20.6%)	53 (34.2%)	15 (30.6%)	0.002
Lung disease	91 (17.3%)	42 (23.7%)	15 (27.3%)	0.056
Known chronic renal disease	6 (1.2%)	23 (13.9%)	30 (58.8%)	< 0.001
Obesity	85 (16.1%)	31 (17.5%)	16 (29.0%)	0.005
Cardiovascular disease	88 (16.7%)	84 (47.5%)	26 (47.3%)	< 0.001
Cerebrovascular disease	32 (6.4%)	38 (23.0%)	10 (18.5%)	< 0.001
Any cancer	64 (12.2%)	32 (18.1%)	11 (20.0%)	0.064
Previous statin treatment	37 (8.9%)	30 (25.4%)	6 (16.7%)	0.006
Previous antiaggregant treatment	59 (11.6%)	52 (31.0%)	15 (27.8%)	< 0.001
Previous anticoagulant treatment	44 (8.8%)	43 (25.3%)	12 (23.1%)	< 0.001
Previous RAAS inhibitors treatment	141 (27.4%)	109 (63.7%)	33 (61.1%)	< 0.001
Asymptomatic	9 (1.7%)	7 (4.0%)	1 (1.9%)	0.226
Shortness of breath	294 (55.8%)	106 (59.8%)	37 (67.2%)	0.003
Anosmia	22 (5.0%)	1 (0.7%)	2 (2.1%)	0.011
Dysgeusia	24 (5.4%)	0 (0.0%)	1 (1.8%)	0.004
Sorethroat	43 (9.5%)	14 (9.0%)	3 (6.7%)	0.820
Fever (> 38.2 °C)	434 (84.4%)	138(78.9%)	38 (70.4%)	0.016
Cough	373 (73.0%)	110 (63.6%)	27 (52.9%)	0.002
Diarrhea	81 (17.2%)	15 (9.4%)	9 (19.1%)	0.051
Myalgias or arthralgias	161 (33.6%)	43 (25.9%)	6 (12.2%)	0.003
Tachypnea	87 (19.0%)	50 (28.1%)	26 (39.9%)	< 0.001
Saturation on admission < 92%	153 (30.5%)	104 (59.8%)	28 (52.8%)	< 0.001
D-Dimer elevation	260 (61.0%)	115 (79.9%)	25 (65.8%)	< 0.001
Procalcitonin elevation	75 (19.5%)	36 (26.5%)	19 (48.7%)	< 0.001
PCR elevation	463 (90.6%)	165 (95.4%)	53 (96.4%)	0.063
Transaminases elevation	185 (41.8%)	67 (42.9%)	20 (41.7%)	0.966
Ferritin elevation	160 (56.9%)	64 (60.4%)	19 (67.9%)	0.485
Lactate dehydrogenase elevation	310 (71.8%)	107 (78.7%)	33 (73.3%)	0.281
Onset creatinine levels (mg/dL)	0.8 ± 0.2	1.4 ± 0.3	3.2 ± 2.0	< 0.001
Total onset lymphocytes count (/UL)	1261 ± 1390	1202 ± 2130	870 ± 514	0.264
Duration from illness onset to first admission	6.5 ± 6.0	4.9 ± 4.1	4.4 ± 3.2	0.001
Acute kidney injury	33 (6.7%)	72 (43.4%)	44 (86.3%)	< 0.001
Bilateral pneumonia	349 (66.3%)	127 (71.8%)	36 (40.8%)	0.311
Sepsis	57 (11.9%)	42 (26.4%)	20 (40.8%)	< 0.001
Ischemic event	2 (0.4%)	2 (1.3%)	0 (0.0%)	0.438
Respiratory insufficiency	176 (35.4%)	122 (72.2%)	31(62.0%)	< 0.001
High Flow Nasal Cannula	120 (24.1%)	63 (37.3%)	25 (48.1%)	< 0.001
Non-invasive mechanical ventilation	80 (16.1%)	44 (26.2%)	11 (20.4%)	0.015
Invasive mechanical ventilation	19 (4.0%)	12 (7.5%)	2 (4.2%)	0.198
Use of corticoids	79 (16.3%)	48 (29.3%)	6 (11.8%)	< 0.001
Use of hydroxychloroquine	408 (82.3%)	130 (76.5%)	33 (63.5%)	0.003
Use of antiviral drugs	357 (71.3%)	108 (63.9%)	29 (58.0%)	0.050
Use of interferon or similar	66 (13.7%)	27 (16.4%)	6 (12.2%)	0.642

Table 1 (continued)

	eGFR > 60 mL/min/1.73 m^2 (N = 526)	eGFR 30–60 mL/min/1.73 m^2 (N = 177)	eGFR < 30 mL/min/1.73 m^2 (N = 55)	p
Use of tocilizumab or similar	26 (5.4%)	15 (9.2%)	1 (2.0%)	0.099
Use of antibiotics	346 (68.8%)	127 (74.7%)	40(76.9%)	0.204
ACEI ARBS during in hospital stay	57 (12.4%)	28 (19.3%)	10 (22.2%)	0.038
Hospitalization stay (days)	6.5 ± 4.3	6.7 ± 4.8	5.7 ± 4.8	0.395

eGFR estimated glomerular filtration rate

observe that a 5.2% of the patients in eGFR > 60 group presented a worsening of their renal function vs 31.8% in eGFR 30–60 group vs 56.0% in eGFR < 30 group, p < 0.001.

Mortality risk assessment

Kaplan–Meier survival landmark analysis according to the glomerular filtration rate are shown in Fig. 1, log-rank test global p < 0.001 and log-rank test between each group. p < 0.001. We investigated those factors associated with a higher risk of suffering from the primary outcome defined as in-hospital mortality. Univariate regression analyses are shown in Supplementary Table 1. After univariate analyses, we performed a Cox multivariate regression analysis to identify those variables that were independently associated with a greater risk of in-hospital mortality. Most relevant risk-factors on admission for in-hospital death (Table 2) in the logistic regression model were: age, hypertension, kidney function, the presence of O2 saturation less than 92% and an elevated lactate dehydrogenase. Renal function at admission behaved as an independent prognostic factor when it was categorically evaluated (eGFR groups) and when it was assessed as a continuous variable (creatinine value at admission), Table S2. The impact of creatinine clearance on mortality is displayed graphically in Fig. 2. As creatinine clearance decreased, the probability of death increased. Importantly, when we excluded patients with known chronic

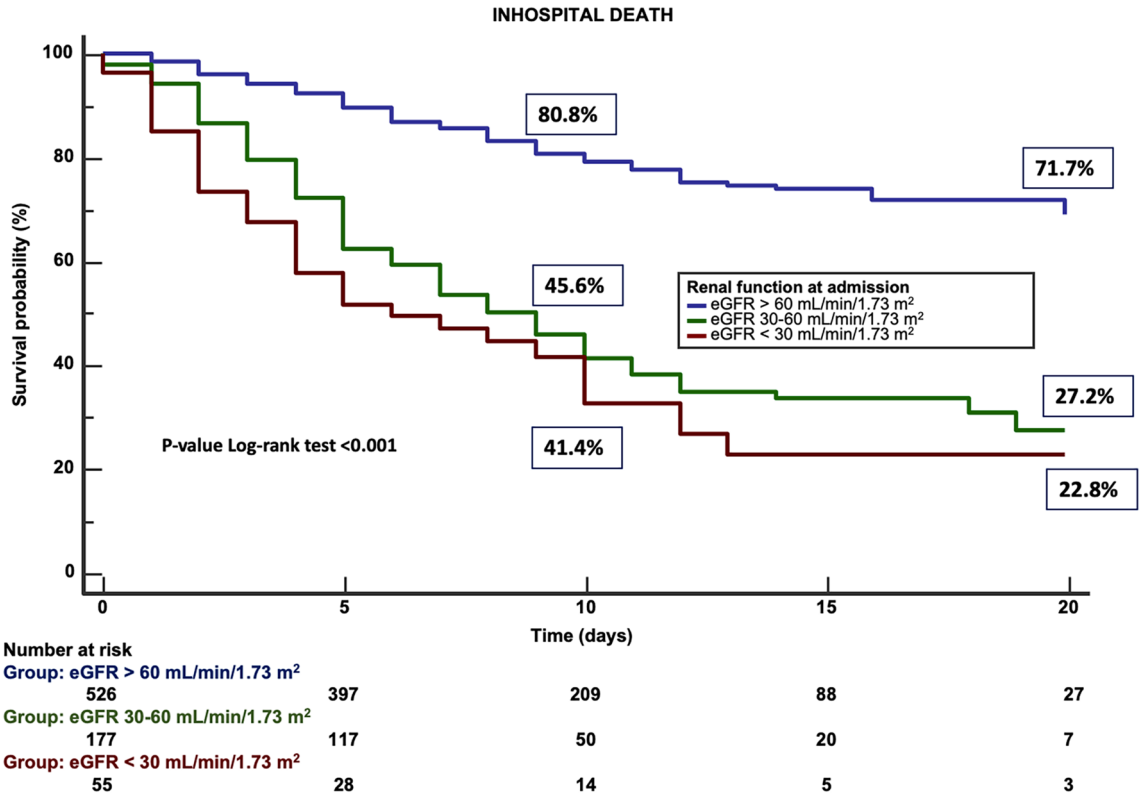

Fig. 1 Kaplan–Meier survival landmark analysis according to the glomerular filtration rate

Table 2 Cox multivariate regression analysis regarding risk factors on admission associated with in-hospital death

	HR (CI 95%)	p
Hypertension	1.642 (1.105–2.179)	0.038
Age	1.034 (1.021–1.048)	< 0.001
Saturation on admission < 92%	3.310 (2.362-4.369)	< 0.001
Lactate dehydrogenase elevation	1.768 (1.161–2.690)	0.008
eGFR 30-60 mL/min/1.73 m^{2a}	2.205 (1.573–3.091)	< 0.001
eGFR < 30 mL/min/1.73 m^{2a}	4.925 (2.152–5.244)	< 0.001

RASS renin–angiotensin–aldosterone system

[a]Reference to eGFR > 60 mL/min/1.73 m^2 group

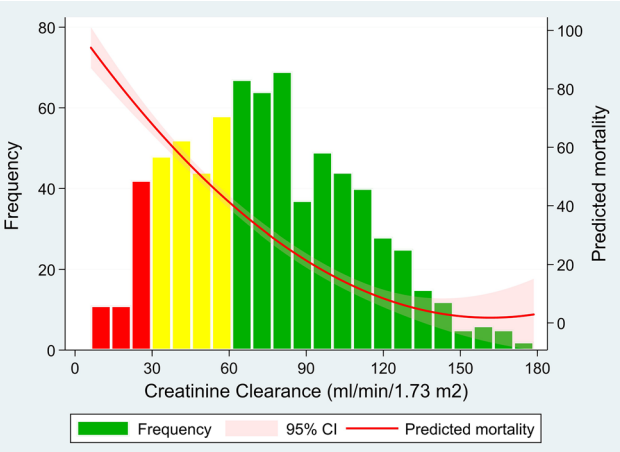

Fig. 2 Association between creatinine clearance and predicted mortality. The predicted probability of all-cause death (red line) is shown, together with 95% confidence interval, after adjustment for age, hypertension, diabetes, dislipemia, smoking habit, any heart disease, any lung disease, any cerebrovascular disease, any immunosuppression condition, RAAS inhibitors treatment, aspirin treatment, anticoagulation treatment, statin treatment, saturation O2 < 92% on admission, D-dimer elevation, PCR elevation, and lactate dehydrogenase elevation at admission. The x-axis shows the values of creatinine clearance as continuous variable. Histograms show the population distribution according to creatinine clearance levels (color figure online)

renal failure from the analysis the results remained consistent (Table S3).

Because hypertension can act as a confounding factor, a new logistic regression analysis was performed excluding hypertensive patients. The deterioration of renal function continued to be independently associated with a worse prognosis in these group of patients (OR = 8.6, 95% CI 1.8–40.5, p < 0.001 in eGFR < 30 mL/min/1.73 m^2 group; OR = 2.2, 95%CI 0.8–5.9, p = 0.128 in eGFR 30–60 mL/min/1.73 m^2 group; reference > 60 mL/min/1.73 m^2 group).

Discussion

In this large international registry conducted in Europe and America, we observed a high prevalence of kidney disease in hospitalized COVID-19 patients. Close to 30% of them had evidence of kidney disease on admission, with elevated serum creatinine, and this was associated with greater in-hospital mortality. Two factors may have been involved in this. On the one hand, increased susceptibility to infection in patients with CKD, and on the other hand, the acute deterioration of renal function related to COVID-19. One possible explanation of the high prevalence of kidney involvement at hospital admission is that some of the patients with COVID-19 had a past history of CKD. Such patients have a proinflammatory state with functional defects in innate and adaptive immune cell populations [8] and are known to have a higher risk pneumonia [9]. Interestingly, in our registry only 8.5% had a history of CKD, while roughly 35% of all the patients displayed any sort of kidney function deterioration on admission; Hence, there must be a direct causal relation-ship between AKI and COVID-19.

To understand why kidney failure may be a crucial factor in the evolution of patients with SARS-CoV-2 infection, it is important to know the evolution of COVID-19. Acute disease progression can be divided into three distinct phases: an early infection phase, a pulmonary phase, and a severe hyperinflammation phase [10–12]. The greatest susceptibility to infection would focus on this first phase of early infection, during which, the virus infiltrates the lung parenchyma and begins to proliferate. In this phase of infection, the RAAS seems to play a key role. SARS-CoV-2 interacts with the RAAS through angiotensin-converting enzyme 2 (ACE2), an enzyme that physiologically counters RAAS activation but also functions as a receptor for SARS viruses [13]. ACE2 is a type I membrane protein expressed in lung, heart, kidney, and intestine but mainly associated with cardiovascular diseases [13]. Recent human tissue RNA-sequencing data demonstrated that ACE2 expression in the kidneys was nearly 100-fold higher than in the lung [14]. Therefore, kidney disease may be caused by coronavirus entering kidney cells through an ACE2-dependent pathway. Moreover, RAAS activity is clearly increased in patients with CKD, so there is a systemic increase in ACE2 receptors that might be translated into an easier SARS-CoV-2 cell infection.

Another factor that may explain a worse prognosis in patients with kidney damage is that the novel coronavirus

may exert direct cytopathic effects on kidney tissue. This is supported by the detection of polymerase chain reaction fragments of coronavirus blood and urine in patients with the 2003 SARS and COVID-19 viral infections [15–17]. A recent in vitro study concluded that the cytopathic effects of SARS-CoV-2 on podocytes and proximal straight tubule cells may cause AKI in patients with COVID-19, especially in Occidental populations due to the highest expression of the ACE2 receptor in these cells [18]. Recently, Li et al. observed renal structural anomalies by CT scan in 100% of patients infected with SARS-CoV-2 [14], and this direct virus-induced damage has been observed in kidney biopsies performed on patients with COVID-19 [19].

Another proposed mechanism that justifies kidney injury during SARS-CoV-2 infection is cytokine-mediated damage. A non-negligible percentage of patients will develop during the inflammatory phase of the disease an exuberant response, called cytokine storm, resulting in uncontrolled pulmonary inflammation, likely a leading cause of case fatality [13]. Rapid viral replication and cellular damage, viral-mediated ACE2 downregulation and shedding, and antibody dependent enhancement are responsible for aggressive inflammation caused by SARS-CoV-2. The initial onset of rapid viral replication may cause massive epithelial and endothelial cell death and vascular leakage, triggering the production of pro-inflammatory cytokines and chemokines that can cause direct kidney damage through apoptosis of the renal tubular epithelial cells [20]. In clinical practice, an altered kidney function should be given particular attention, as an impaired renal function could be an early marker of a hyperinflammatory phase in a patient who has not yet developed severe respiratory failure, therefore, monitoring kidney function must be emphasized even in patients with mild respiratory symptoms. Early detection of renal abnormalities could involve the early start of drugs against the inflammatory cascade and could help to improve the vital prognosis of COVID-19. Furthermore, it could allow a better treatment adjustment because many of the drugs that are being used for the treatment of COVID-19 are nephrotoxic through pharmacological/iatrogenic mechanisms.

Several publications have associated hypertension with a higher probability of infection and a worse evolution in patients with COVID-19 [21, 22], and our data goes in the same direction. Although hypertension is a highly prevalent cardiovascular risk factor in CKD patients, our data supports that renal failure continues to be an independent prognostic factor irrespective of the presence or absence of concomitant hypertension.

Our findings warn of the possibility that patients with chronic renal failure could be patients at risk for COVID-19 infection. In this sense, recent publications attempt to protocolize the care of CKD patients to reduce the risk of infection [23–25].

Limitations

We need to consider the constraints of a study of this design. It is possible that some incident events in the participating centers have not been diagnosed and/or reported. The calculation of the incidence of the events is not precise since the recruitment was performed in participating centers without other sampling procedure than the broad inclusion criteria (hospital discharge) and would vary depending on the patient´s, hospital, country or local pandemic curve. Regarding the management applied, at all times they were decided by the attending medical team, as well as in the comparison group. The high incidence of respiratory failure could be related to the definition used.

Other considerations to take into account are: an accurate baseline serum creatinine was not available, which may have led to an underestimation of AKI or erroneous associations; although we attempted to adjust for many confounders, other unmeasured or unknown confounders might have played a role; despite we tried to report all the treatments used during admission, the protocols between the centers were different, which may influence the results. The precise impact of COVID-19 on kidney structure and function and the incidence of CKD in these patients warrant further investigation.

Conclusions

Our findings show the prevalence of AKI on admission in patients with COVID-19 is high and is associated with a greater in-hospital mortality rate. Physicians should closely monitor any patient with impaired renal function on admission, regardless of respiratory status. Our data comes from a multicenter registry and therefore does not allow to have a precise mortality risk assessment. More studies are needed to confirm these findings.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the Ethics Research Committee from Hospital Clinico San Carlos (Madrid, Spain) (20/241-E) and the Spanish Drug Agency authorities (AEMPS classification: EPA-0D) and by local committees when needed.

Informed consent Written informed consent was waived owing to the severity of the situation and the use of deidentified retrospective data. However, verbal authorization from either patients or caregivers was required.

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