

# Predictors of Mortality in COVID-19 Patients at Kinshasa Medical Center and A Survival Analysis: A Retrospective Cohort Study

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**Research article**

**Keywords:** COVID-19, Mortality, African people, Procalcitonine, acute kidney injury

**Posted Date:** January 28th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-153818/v1>

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**Version of Record:** A version of this preprint was published at BMC Infectious Diseases on December 1st, 2021. See the published version at <https://doi.org/10.1186/s12879-021-06984-x>.

# Abstract

## Background

Despite it being a global pandemic, there is little research examining the clinical features of severe COVID-19 in sub-Saharan Africa. This study aims to identify predictors of mortality in COVID-19 patients in an African setting.

## Methods

In this retrospective, observational, cohort study carried out at the Kinshasa Medical Centre (KMC) between March 10, 2020 and July 10, 2020, we included all adult inpatients ( $\geq 18$  years old) with a laboratory diagnosis by PCR of COVID-19. The end point of the study was survival to discharge (time-to-death). The study population was dichotomized into survivors and non-survivors group. Kaplan-Meier plot was used for survival analyses. The Log-Rank test was employed to compare the survival curves. Predictors of mortality were identified by Cox regression models. The significance level of P value was set at 0.05.

## Results

106 patients (mean age  $55.6 \pm 13.2$  years old, 80.2% were male), were included in this study, of whom 34 (32 %) died during their hospitalisation. The main Complications of the patients included ARDS in 59/66 (89.4%) patients, coagulopathy in 35/93 (37.6%) patients, acute cardiac injury in 24/98 (24.5%) patients, AKI in 15/74 (20.3%) patients and secondary infection in 12/81 (14.8%) patients. The independent predictors of mortality were found to be age  $\geq 65$  years [aHR 2.49; 95% CI: 1.53-5.69], AKI stage 3 [aHR 2.51; 95% CI: 1.33-6.80], proteinuria [aHR 2.60; 95% CI: 1.40-6.42], CRP  $>150$  mg/L [aHR 2.75; 95% CI: 1.29-3.68] and procalcitonin (PCT)  $> 0.5$  ng/ml [aHR 3.20; 95% CI: 1.70-7.49]. The median survival time of the entire group was 12 days. The cumulative survival rate of COVID-19 patients was 86.9%, 65.0% and 19.9% respectively at 5, 10 and 20 days. Levels of creatinine ( $p= 0.012$ ), were clearly elevated in non-survivors compared with survivors throughout the clinical course and increased deterioration.

## Conclusion

The results from this study demonstrated that an advanced age, proteinuria, AKI and raised CRP and PCT offered a worse prognosis in COVID-19 patients. In addition, serum levels of creatinine significantly rose during admission in the non-survivor group compared with those who survived to discharge.

## Background

In December 2019, the first case of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) virus was detected in China (1). Three months later, due to its rapid global spread, the World Health Organization (WHO) declared the outbreak a pandemic (1). By the end of September 2020, the WHO had reported that SARS-COV-2 had infected at least

32.7 million people and was responsible for the deaths of more than one million (2). The clinical manifestations of this new disease vary widely in severity; ranging from no or mild symptoms to patients with pneumonia progressing rapidly to acute respiratory distress syndrome (ARDS), multi-organ failure and death (3). There is not only a huge disparity in the severity of this disease but also in its impact globally. From the onset of the pandemic, international health organisations predicted high morbidity and mortality rates in African countries. However, this has not transpired, with Africa reporting much lower rates than most of the rest of the world (4, 6, 7). Notwithstanding the huge amount of global research investigating these morbidity and mortality disparities, most of these data emanate from non-African countries.

The Democratic Republic of Congo (DRC) situated in Central Africa, is a vast country with a surface area equivalent to Western Europe with a population of 89,561,403 (4). The country reported its first case of COVID-19 on March 10, 2020 in a person recently arrived from France (5). As of September 27, 2020, there have been a total of 10, 592 positive cases, with a mortality of 271(2). To date there is a paucity of research on COVID-19 from the DRC, two papers have been identified. The objective of this report is to evaluate the risk factors for COVID-19 related mortality by comparing the demographic and clinical characteristics of patients diagnosed with COVID-19 admitted to the Kinshasa Medical Centre (KMC), located in Kinshasa, the capital of the Democratic Republic of Congo (DRC).

## **Methods**

### **Study design, setting and population**

This retrospective, observational, cohort study was carried out at the KMC, a private hospital officially designated for the treatment of COVID-19. We enrolled 106 patients who were admitted and managed in the KMC between March 10, 2020 and July 10, 2020. The inclusion criteria were strictly based on laboratory confirmation of SARS-CoV-2 by qualitative reverse-transcriptase polymerase chain reaction (RT-PCR) assay of nasopharyngeal swabs. Only patients who demonstrated signs of moderate to severe illness were admitted to hospital. There was no formal determination of sample size and all patients meeting the inclusion criteria were recruited.

### **Ethics approval**

This study was carried out in strict compliance with the recommendations of the Declaration of Helsinki III (8). The files were looked was designed anonymously. The information obtained during the history and clinical examination was transcribed into pre-established and pre-coded investigation sheets while respecting the confidentiality and privacy of patients. Our research projects on Covid-19 had been authorized by the National Ethics committee of Health, Democratic Republic of Congo (N°225/CNES/BN/PMMF/2020). Written, informed was waived by the National Ethics committee of Health, Democratic Republic of Congo because of the urgency and unprecedented nature of the COVID-19 pandemic.

# Data collection

Clinical data were extracted manually from the KMC electronic patient database. Information about demographic characteristics (age and gender); the existence of any chronic conditions (hypertension, diabetes mellitus, chronic kidney disease); initial symptoms (fever, cough, shortness of breath, chills, dyspnea, fatigue, nausea, vomiting, and diarrhea); vital signs (temperature, respiratory rate [RR], heart rate [HR], and blood oxygen saturation [BOS]); and laboratory tests (haemoglobin [Hb], white blood cells [WBC], neutrophils, lymphocytes, platelets, albumin, creatinine, urea, lactate dehydrogenase [LDH], creatine kinase [CK], D-dimer, C-reactive protein [CRP], procalcitonin [PCT], fibrinogen, high sensitivity Troponin I [hsTNI], electrolytes) and thoracic computerized tomography scan (CT) score were all collected from the time of the admission. In addition we collected information about the treatment received (administration of antibiotics, corticosteroids, oxygen therapy, mechanical ventilation or haemodialysis, complications, and outcomes during the hospital admission.

## Definitions:

Fever was defined as axillary temperature of at least 37.3 °C. Hypertension was recorded if the patient was taking any antihypertensive drug or had two separate BP measurements  $\geq 140/90$  mmHg (9). Secondary infection was diagnosed when patients showed clinical symptoms or signs of pneumonia or bacteraemia and a positive culture of a new pathogen was obtained from blood samples after admission (10). The diabetes diagnosis was based on criteria from the American Diabetes Association as a presence of a fasting plasma glucose level of  $> 126$  mg/dL or usage of antidiabetic drug (11). CKD was defined according to KDIGO definition (12). ARDS was defined according to the Berlin Definition (13). Acute Kidney Injury (AKI) was diagnosed according to KDIGO clinical practice guidelines based on the serum creatinine levels (14). Acute cardiac injury was diagnosed if the serum concentration of HsTNI was above the upper limit of the reference range ( $> 28$  pg/mL) (15). Coagulopathy was defined as a prothrombin time ratio (PT<sub>r</sub>) of less than 70% (16).

On admission each patient had a thoracic CT scan that was assessed for severity of pulmonary involvement. A semi-quantitative CT scoring system was calculated based on the extent of lobar involvement (0:0%; 1: $< 5\%$ ; 2:5–25%; 3:26–50%; 4:51–75%; 5:  $> 76\%$ ) (17).

## Statistical analysis

The study population was dichotomized into survivors and non-survivors group. Data were expressed as mean  $\pm$  standard deviation, or median (range) for continuous variables and number (%) for categorical variables. The Mantel-Haenszel Chi-squared test was used to compare proportions with application of the exact Fisher test and the corrected Yates test, where appropriate. Student's t-test and analysis of variance (ANOVA) were used to compare the means of two or more groups with normal distributions, respectively. Mann-Whitney U test and Kruskal Wallis U test were applied for skewed distribution. Statistical analyses were performed using SPSS version 21 for Windows (SPSS Inc, Chicago, IL) and stata version 13. Laboratory values in survivors and non-survivors for the first 7 days after admission were assessed.

Survival was defined as the time period between hospital admission and death or the end of the study. Kaplan-Meier plot was used for survival analyses. The Log-Rank test was employed to compare the survival curves. Predictors of mortality were assessed using Cox regression models. The significance level of P value was set at 0.05.

## Results

Between March, 10, 2020 and July, 10, 2020, at the KMC a total of 432 patients with confirmed COVID-19 were identified, of whom 106 (24.5%) were critically ill, as defined by the presence of any organ failure. The baseline characteristics of these 106 patients are summarised in Table 1 and their laboratory findings and chest CT scan score in Table 2. 34 patients died during hospitalisation and 72 were discharged. The mean age of the admitted patients was  $55.6 \pm 13.2$  years, including 26 (24.5%) patients over 65 years old. The majority were male (80.2%) with hypertension being the main comorbidity in 62 (58.2%) patients. The median (IQR) time from COVID-19 symptoms onset to hospital admission was 7 (5.8–10.0) days, whereas the median time to death was 22.0 (14.0–33.0). Fever and cough were the most common initial symptoms (65.1% and 55.7%, respectively). On admission, the median axillary temperature was  $37.1$  °C (IQR: 36.6–38.3 °C). The median respiratory rate was 22/min (IQR: 20–29/min) and median blood oxygen saturation on room air was 89% (IQR: 82–92%). Compared between the two groups, the patients in non-survivors group had significantly higher age ( $61.3 \pm 12$  vs  $52.9 \pm 13$ ), Systolic Blood Pressure ( $145.5 \pm 17.4$  vs  $137.0 \pm 17$ ), Lactate dehydrogenase (604 [244–874.8] vs 362.5 [228.3–551.8]), HDL cholesterol (1.19[0.75–1.55] vs 0.85 [0.66–1.08]), troponin (20.8[10.3–90.5] vs 4.9[2.0–16.9]), procalcitonin (0.360 [0.185–2.583] vs 0.140 [0.06–0.440]) and lower PaO<sub>2</sub>/FiO<sub>2</sub> ratio (67.6[57.9–96.5] vs 145.5 [73.1–251.2]). The patients in non-survivors group had also significantly more count of neutrophil (5120.5 [3748–7815] vs 3555.7 [2630–5911.5]) (Table 2). The frequency of complications were higher in non-survivors than survivors (Table 3). The main Complications of the patients included ARDS in 59/66 (89.4%) patients, coagulopathy in 35/93 (37.6%) patients, acute cardiac injury in 24/98 (24.5%) patients, AKI in 15/74 (20.3%) patients and secondary infection in 12/81 (14.8%) patients (Table 3). All 28 (26.4%) patients who required mechanical ventilation (MV) died. The median time from illness onset to invasive mechanical ventilation was 15 days (9.0–22.0). 14 (13.2%) patients received renal replacement therapy. Some laboratory parameters were tracked from illness onset (Fig. 1). Levels of CRP, PCT and creatinine were clearly elevated in non-survivors compared with survivors throughout the clinical course and increased deterioration (Fig. 1). As of July 10, 2020, 34 (32.0%) patients had died; of those that died a total of 17.6% (6/34) had secondary infections. The main germs found were *Staphylococcus haemolyticus* (Fig. 2). The median (IQR) length of stay from hospitalization to discharge was 18(15–22) days, while the median (IQR) time from hospitalization to death was 22 (14–33) days. Kaplan Meir survival curve of the study population is illustrated in Fig. 3. The median survival time of the entire group was 12 days. The cumulative survival rate of COVID-19 patients was 86.9%, 65.0% and 19.9% respectively at 5, 10 and 20 days. The Kaplan-Meier curves showed a better survival in younger patients, in patients with No AKI and in patients who have a procalcitonin level below 0.5 (Fig. 4). Multivariable analysis (Table 4) showed age  $\geq 65$  years [aHR 2.49; 95% CI: 1.53–5.69], AKI stage 3 [aHR 2.51; 95% CI: 1.33–6.80], proteinuria [aHR 2.60; 95% CI: 1.40–6.42], CRP > 150 mg/L [aHR 2.75; 95% CI: 1.29–3.68] and

procalcitonin (PCT) > 0.5 ng/ml [aHR 3.20; 95% CI: 1.70–7.49] as predictors independently associated with an increased risk of mortality.

Table 1  
Clinical features at admission

|   | Total (n = 106)  | Non-survivors (n = 34) | Survivors (n = 72) | p-value |
|---|------------------|------------------------|--------------------|---------|
| Age, years  | 55.6 ± 13.2      | 61.3 ± 12.0            | 52.9 ± 13.0        | 0.002   |
| > 65 years  | 26 (24.5)        | 15 (44.1)              | 11 (15.3)          | 0.001   |
| Sex   |                  |                        |                    | 0.701   |
| Females   | 21(19.8)         | 6 (17.6)               | 15 (20.8)          |         |
| Males   | 85(80.2)         | 28 (82.4)              | 57 (79.2)          |         |
| Comorbidities   |                  |                        |                    |         |
| Hypertension  | 62 (58.5)        | 21 (61.8)              | 41 (56.9)          | 0.638   |
| Diabetes melitus  | 35(33.0)         | 14 (41.2)              | 21 (29.2)          | 0.220   |
| CKD   | 5 (4.7)          | 2 (5.9)                | 3 (4.2)            | 0.697   |
| SBP, mm Hg  | 139.8 ± 17.5     | 145.5 ± 17.4           | 137.0 ± 17.0       | 0.036   |
| DBP, mm Hg  | 84.9 ± 13.9      | 87.0 ± 17.6            | 83.8 ± 11.7        | 0.327   |
| HR,bpm  | 92.1 ± 15.1      | 93.6 ± 17.5            | 91.3 ± 14.0        | 0.513   |
| RR, cycle/min   | 22.0 (20.0–29.0) | 27.5 (22.0–35.0)       | 20.0 (20.0–26.0)   | 0.002   |
| RR > 24 cycles/min  | 26 (36.6)        | 14 (58.3)              | 12 (25.5)          | 0.007   |
| T, °C   | 37.1 (36.6–38.3) | 37.5 (36.6–38.5)       | 37.0 (36.6–38.0)   | 0.178   |
| Fever   | 69 (65.1)        | 22 (64.7)              | 47 (65.3)          | 0.954   |
| Cough   | 59 (55.7)        | 22 (64.7)              | 37 (51.4)          | 0.198   |
| Dyspnea   | 42 (39.6)        | 14 (41.2)              | 28 (38.9)          | 0.822   |
| Asthenia  | 42 (39.6)        | 11 (32.4)              | 31 (43.1)          | 0.293   |
| Symptoms, days  | 7.0 (5.8–10.0)   | 7.0 (5.0–10.0)         | 7.0 (6.0–8.5)      | 0.682   |
| Data are mean ± standard, median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test, $\chi^2$ test, or Fisher's exact test, as appropriate. Bpm = beats per minutes. CKD = Chronic Kidney Disease. DBP = Diastolic Blood Pressure. HR = Heart Rate. RR = Respiratory Rate. $\chi^2$ test comparing all subcategories |                  |                        |                    |         |

Table 2  
Biological and radiological characteristics at admission

| Variable                                  | Total (n = 106)          | Non-survivors (n = 34) | Survivors (n = 72)     | p-value |
|---|--------------------------|------------------------|------------------------|---------|
| Glycemia, mg/dl                           | 124.0 (103.0–176.0)      | 136.5 (100.5–180.8)    | 119.0 (103.5–171.0)    | 0.614   |
| WBC count, x10 <sup>9</sup> per L         | 6155.0 (4775.0 – 8722.5) | 7045.0 (5267.5–9965.0) | 5930.0 (4510.0–8097.5) | 0.056   |
| <4000                                     | 10/91 (11.0)             | 2/27 (7.4)             | 8/64 (12.5)            | 0.617   |
| 4000–10000                                | 80/91 (87.9)             | 25/27 (92.6)           | 55/64 (85.9)           |         |
| >10000                                    | 1/91 (1.1)               | 0/27 (0)               | 1/64 (1.6)             |         |
| Neutrophils count, x10 <sup>9</sup> per L | 4325.0 (2919.0–6379.2)   | 5120.5 (3748.0–7815.5) | 3555.7 (2630.0–5911.5) | 0.021   |
| Lymphocytes count, x10 <sup>9</sup> per L | 1366.1 (1010.4–1650.0)   | 1220.4 (879.0–1626.9)  | 1382.1 (1070.0–1690.2) | 0.193   |
| <800                                      | 13/103 (12.6)            | 7/33 (21.2)            | 6/70 (8.6)             | 0.071   |
| Hb, g/dl                                  | 13.2 ± 2.1               | 12.9 ± 2.2             | 13.3 ± 2.0             | 0.372   |
| ASAT, UI/l                                | 52.0 (28.8–90.3)         | 68.0 (39.5–95.0)       | 50.5 (26.3–86.0)       | 0.124   |
| ALAT, UI/l                                | 35.5 (24.8–68.3)         | 32.5 (24.8–62.8)       | 39.5 (23.5–73.0)       | 0.712   |
| ALAT > 40 UI                              | 48 (45.3)                | 13 (38.2)              | 35 (48.6)              | 0.316   |
| Total Bilirubin, µmol/l                   | 8.0 (6.2–12.0)           | 10.4 (6.2–14.2)        | 7.7 (5.9–10.7)         | 0.123   |
| Direct Bilirubin, µmol/l                  | 4.3 (3.0–6.1)            | 5.7 (3.2–7.7)          | 3.8 (2.9–5.8)          | 0.059   |
| Pro BNP, pg/ml                            | 119.5 (45.0–633.8)       | 279.5 (47.3–1355.3)    | 98.0 (38.3–378.3)      | 0.028   |
| Ferritin, ng/ml                           | 1200.0 (565.4–1200.0)    | 1200.0 (842.5–1200.0)  | 1200.0 (527.1–1200.0)  | 0.377   |
| Na <sup>+</sup> , mmol/l                  | 137.9 ± 4.4              | 137.6 ± 5.8            | 138.1 ± 3.7            | 0.593   |
| K <sup>+</sup> , mmol/l                   | 3.8 ± 0.5                | 3.8 ± 0.5              | 3.8 ± 0.4              | 0.934   |
| HbA1c, %                                  | 8.3 ± 2.7                | 8.1 ± 2.7              | 8.4 ± 2.8              | 0.737   |

Data are mean ± standard, median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test,  $\chi^2$  test, or Fisher's exact test, as appropriate. ALAT = Alanina Amino Transferase. ASAT = Aspartate Amino transferase. CRP = C reactive protein. Hb = Hemoglobin. HDLc = High density Lipoprotein cholesterol. LDH = Lactate dehydrogenase. CK = Creatinine kinase. Pro BNP = Brain Natriuretic peptide. PTR = Prothrombine Time ratio. PCT = Procalcitonin. TC = Total Cholesterol. WBC = White Blood Cell.

| Variable                     | Total (n = 106)       | Non-survivors (n = 34) | Survivors (n = 72)    | p-value  |
|------------------------------|-----------------------|------------------------|-----------------------|----------|
| Creatinin, $\mu\text{mol/l}$ | 89.5 (74.0–110.3)     | 100.5 (74.8–125.5)     | 85.5 (74.0–105.3)     | 0.164    |
| LDH, UI/l                    | 410.0 (232.0–656.3)   | 604.0 (244.0–874.8)    | 362.5 (228.3–551.8)   | 0.026    |
| >245                         | 68/98 (69.4)          | 23/30 (76.7)           | 45/68 (66.2)          | 0.299    |
| CK, UI/l                     | 199.0 (96.0–398.0)    | 274.0 (99.5–485.8)     | 163.0 (93.0–354.0)    | 0.214    |
| >185                         | 46/91 (50.5)          | 18/28 (64.3)           | 28/63 (44.4)          | 0.081    |
| TC, mmol/l                   | 4.2 (3.3–5.6)         | 4.2 (3.3–5.7)          | 4.3 (3.2–5.5)         | 0.927    |
| HDLc, mmol/l                 | 0.93 (0.67–1.24)      | 1.19 (0.75–1.55)       | 0.85 (0.66–1.08)      | 0.047    |
| Triglycerids, mmol/l         | 1.40 (0.94–2.19)      | 1.51 (0.79–2.15)       | 1.36 (1.09–2.38)      | 0.430    |
| Troponin, ng/l               | 9.9 (3.2–27.9)        | 20.8 (10.3–90.5)       | 4.9 (2.0–16.9)        | < 0.0001 |
| >28                          | 24/98 (24.5)          | 14/34 (41.2)           | 10/64 (15.6)          | 0.005    |
| PTr, %                       | 74.3 $\pm$ 16.6       | 75.4 $\pm$ 17.0        | 73.8 $\pm$ 16.6       | 0.674    |
| <70                          | 35/93 (37.6)          | 11/28 (39.3)           | 24/65 (36.9)          | 0.829    |
| $\geq$ 70                    | 58/93 (62.4)          | 17/28 (60.7)           | 41/65 (63.1)          |          |
| D-dimer, ng/ml               | 1603.5 (795.3–4093.3) | 1694.2 (921.6–5482.1)  | 1593.3 (744.5–3329.7) | 0.430    |
| $\leq$ 500                   | 14/97 (14.4)          | 5/31 (16.1)            | 9/66 (13.6)           | 0.305    |
| >500 - $\leq$ 1000           | 18/97 (18.6)          | 3/31 (9.7)             | 15/66 (22.7)          |          |
| >1000                        | 65/97 (67.0)          | 23/31 (74.2)           | 42/66 (63.6)          |          |
| Fibrinogen, g/l              | 7.3 (5.4–8.4)         | 7.4 (6.3–9.1)          | 7.2 (5.2–8.2)         | 0.254    |
| CRP, mg/l                    | 125.0 (53.0–218.0)    | 209.5 (107.0–309.3)    | 95.5 (29.5–187.8)     | < 0.0001 |
| PCT, ng/ml                   | 0.200 (0.095–0.620)   | 0.360 (0.185–2.503)    | 0.140 (0.060–0.440)   | < 0.0001 |
| <0.1                         | 26 (24.8)             | 1 (2.9)                | 25 (35.2)             | 0.002    |

Data are mean  $\pm$  standard, median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test,  $\chi^2$  test, or Fisher's exact test, as appropriate. ALAT = Alanina Amino Transferase. ASAT = Aspartate Amino transferase. CRP = C reactive protein. Hb = Hemoglobin. HDLc = High density Lipoprotein cholesterol. LDH = Lactate dehydrogenase. CK = Creatinine kinase. Pro BNP = Brain Natriuretic peptide. PTR = Prothrombine Time ratio. PCT = Procalcitonin. TC = Total Cholesterol. WBC = White Blood Cell.

| Variable   | Total (n = 106)    | Non-survivors (n = 34) | Survivors (n = 72) | p-value  |
|--|--------------------|------------------------|--------------------|----------|
| 0.1 - <0.25  | 30 (28.6)          | 11 (32.4)              | 19 (26.8)          |          |
| 0.25 - <0.5  | 18 (17.1)          | 6 (17.6)               | 12 (16.9)          |          |
| ≥ 0.5  | 31 (29.5)          | 16 (47.1)              | 15 (21.1)          |          |
| PaO <sub>2</sub> /FiO <sub>2</sub>   | 100.2 (63.2–209.4) | 67.6 (57.9–96.5)       | 145.5 (73.1–251.2) | 0.001    |
| TDM Score  |                    |                        |                    |          |
| Normal   | 3/92 (3.3)         | 0/27 (0)               | 3/65 (4.6)         | < 0.0001 |
| Score 1  | 11/92 (12.0)       | 0/27 (0)               | 11/65 (16.9)       |          |
| Score 2  | 17/92 (18.5)       | 3/27 (11.1)            | 14/65 (21.5)       |          |
| Score 3  | 27/92 (29.3)       | 4/27 (14.8)            | 23/65 (35.4)       |          |
| Score 4  | 22/92 (23.9)       | 11/27 (40.7)           | 11/65 (16.9)       |          |
| Score 5  | 12/92 (13.0)       | 9/27 (33.3)            | 3/65 (4.6)         |          |
| Data are mean ± standard, median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test, $\chi^2$ test, or Fisher's exact test, as appropriate. ALAT = Alanina Amino Transferase. ASAT = Aspartate Amino transferase. CRP = C reactive protein. Hb = Hemoglobin. HDLc = High density Lipoprotein cholesterol. LDH = Lactate dehydrogenase. CK = Creatinine kinase. Pro BNP = Brain Natriuretic peptide. PTR = Prothrombine Time ratio. PCT = Procalcitonin. TC = Total Cholesterol. WBC = White Blood Cell. |                    |                        |                    |          |

Table 3  
Patients management and evolution

| Variable                               | Total (n = 106) | Non-survivors (n = 34) | Survivors (n = 72) | p-value  |
|--|-----------------|------------------------|--------------------|----------|
| Oxygenotherapy at admission            |                 |                        |                    |          |
| Ambient air                            | 10 (9.5)        | 0 (0)                  | 10 (14.1)          | < 0.0001 |
| Nasal cannula oxygenotherapy           | 18 (17.1)       | 2 (5.9)                | 16 (22.5)          |          |
| High concentration oxygen masks        | 68 (64.8)       | 24 (70.6)              | 44 (62.0)          |          |
| Non invasive ventilation               | 9 (8.6)         | 8 (23.5)               | 1 (1.4)            |          |
| ARDS severity                          |                 |                        |                    |          |
| No ARDS                                | 7/66 (10.6)     | 0/24 (0)               | 7/42 (16.7)        | 0.003    |
| Mild ARDS                              | 11/66 (16.7)    | 2/24 (8.3)             | 9/42 (21.4)        |          |
| Moderate ARDS                          | 15/66 (22.7)    | 3/24 (12.5)            | 12/42 (28.6)       |          |
| Severe ARDS                            | 33/66 (50.0)    | 19/24 (79.2)           | 14/42 (33.3)       |          |
| AKI                                    | 15/74 (20.3)    | 12/30 (40.0)           | 3/44 (6.8)         | < 0.0001 |
| Hemodialysis                           | 14 (13.2)       | 13 (38.2)              | 1 (1.4)            | < 0.0001 |
| ARDS                                   | 59/66 (89.4)    | 24/24 (100)            | 35/42 (83.3)       | 0.034    |
| Mechanical ventilation                 | 28 (26.4)       | 28 (82.3)              | 0 (0)              | < 0.0001 |
| Vasopressors use                       | 9/90 (10)       | 9/28 (32.1)            | 0/62 (0)           | < 0.0001 |
| Delay from symptoms onset to :         |                 |                        |                    |          |
| Corticosteroids start, day             | 10.0 (7.0–15.0) | 11.0 (8.0–13.0)        | 10.0 (6.0–15.0)    | 0.495    |
| NIV initiation, day                    | 12.0 (7.0–13.0) | 12.0 (7.0–13.0)        | --                 | --       |
| Mechanical Ventilation initiation, day | 15.0 (9.0–22.0) | 15.0 (9.0–22.0)        | --                 | --       |

Data are median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test,  $\chi^2$  test, or Fisher's exact test, as appropriate. AKI = Acute Kidney Injury. ARDS = Acute Respiratory Distress Syndrom. NIV = Non-Invasive Ventilation

| Variable   | Total (n = 106)  | Non-survivors (n = 34) | Survivors (n = 72) | p-value |
|--|------------------|------------------------|--------------------|---------|
| Death or discharge, day  | 19.0 (15.0–26.0) | 22.0 (14.0–33.0)       | 18.0 (15.0–22.0)   | 0.113   |
| <p>Data are median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test, <math>\chi^2</math> test, or Fisher's exact test, as appropriate. AKI = Acute Kidney Injury. ARDS = Acute Respiratory Distress Syndrom. NIV = Non-Invasive Ventialtion</p> |                  |                        |                    |         |

Table 4  
Predictors of mortality in COVID-19 patients.

| Variable  | Unadjusted HR (95%CI) | p            | Adjusted HR (95% CI) | p            |
|---|-----------------------|--------------|----------------------|--------------|
| Age > 65 years  |                       |              |                      |              |
| No  | 1                     |              | 1                    |              |
| Yes   | 3.44 (1.51–7.86)      | <b>0.003</b> | 2.49 (1.53–5.69)     | <b>0.025</b> |
| Proteuneria   |                       |              |                      |              |
| Negative  | 1                     |              | 1                    |              |
| Positive  | 3.72 (1.27–10.94)     | <b>0.017</b> | 2.60 (1.40–6.42)     | <b>0.009</b> |
| RR > 24 bpm   |                       |              |                      |              |
| No  | 1                     |              | 1                    |              |
| Yes   | 2.56 (1.04–6.29)      | <b>0.040</b> | 1.50 (0.67–6.14)     | 0.575        |
| Troponine > 28 ng/ml  |                       |              |                      |              |
| No  | 1                     |              | 1                    |              |
| Yes   | 2.32 (1.01–5.37)      | <b>0.049</b> | 1.79 (0.35–9.10)     | 0.481        |
| CRP > 150 mg/dl   |                       |              |                      |              |
| No  | 1                     |              | 1                    |              |
| Yes   | 2.88 (1.22–6.81)      | <b>0.016</b> | 2.75 (1.29–3.68)     | <b>0.007</b> |
| AKI   |                       |              |                      |              |
| No AKI  | 1                     |              | 1                    |              |
| AKI 2   | 2.61 (0.86–7.97)      | <b>0.091</b> | 0.91 (0.26–3.26)     | 0.890        |
| AKI 3   | 4.47 (1.59–12.58)     | <b>0.005</b> | 2.51 (1.33–6.80)     | <b>0.016</b> |
| PCT > 0.5 ng/ml   |                       |              |                      |              |
| No  | 1                     |              | 1                    |              |
| Yes   | 3.40 (1.47–7.88)      | <b>0.004</b> | 3.20 (1.70–7.49)     | <b>0.013</b> |
| AKI = Acute Kidney Injury. RR = Respiratory rate. CRP = C-reactive protein. PCT = Procalcitonin |                       |              |                      |              |

## Discussion

To date, only two studies have been published from the DRC examining patients admitted with COVID-19 (17, 18). Both these studies were limited by a lack of robust analysis of biological and laboratory

parameters that might predict hospital mortality in COVID-19 (5, 18). Our retrospective cohort study, carried out in the DRC, aims to add comprehensive data about mortality risk factors for COVID-19. The findings demonstrate that an age greater than 65 years old, AKI stage 3 and a raised serum PCT and CRP level on admission were significant predictors of mortality in COVID-19 patients. Additionally, increasing levels of creatinine during hospital admission were associated with an increased mortality.

Globally, the hospital COVID-19 mortality rates varies between 4 and 70% (19–25). This disparity is partially explained by differences in the epidemiology of the study populations as well as in their hospital management. For example, Du et al demonstrated that older patients with pre-existent co-morbidities had a higher risk of mortality than a younger healthier person (25). Ciceri et al. reported 23% mortality in patients presenting less severe forms on admission (a median oxygen saturation of 93%) (26). In comparison, our study revealed a mortality of 32.0% of whom only 24.5% had an age > 65 years, and had few comorbidities and upon admission had a less severe form of the disease (mean PaO<sub>2</sub> 62.62 ± 14.0 mmHg). In contrast to international studies demonstrating that being male is associated with an increased risk of mortality (27), our findings did not demonstrate any significant gender difference in risk.

As in several previous studies (25–29), in our study an advanced age was associated with increased mortality from COVID-19. This vulnerability amongst the elderly is often explained by immunosenescence that is accompanied by a decrease in the production of native T and B cells as well as a decrease in the function of immune cells participating in innate immunity (28). These changes reduce the effective viral clearance and increase the likelihood of triggering a deregulated immune response in which cytokines are largely released from activated immune cells causing a cytokine storm (28). In addition to immune senescence, there are several other age-related factors such as comorbidities resulting in higher morbidity and mortality (28). In our cohort, the number of comorbidities also increased with age.

Viral infections are not usually associated with a raised serum PCT, a finding supported in current COVID-19 research (30). Procalcitonin, which is the 116-amino acid precursor of the hormone calcitonin, is normally synthesized and released by thyroid parafollicular C cells (30). It can also be synthesized in many extrathyroid tissues during bacterial infection which is mediated by increased concentration of tumor necrosis factor alpha (TNF $\alpha$ ) and interleukin 6 (30). Worldwide, the average PCT level on admission is less than 0.25 ug/L in COVID-19 patients (31). During admission for COVID-19, an increased PCT is explained either by a bacterial hospital acquired co-infection or by a general deterioration of the patient (32). Several studies have reported that elevated PCT is positively associated with the severity of COVID-19 (33–36). Hu et al. describe bacterial co-infection rates, defined by a positive blood culture in 20% of those who were severely unwell and in 50% who were critically unwell. Yet, in 50% of those with severe COVID-19 and in 80% of those critically unwell the PCT was raised (30). In our study, 12/81 (14.8%) of admission blood cultures were positive yet the PCT was raised in 29.5% of those patients. Our study demonstrated that during infection with COVID-19 a progressive elevation of PCT served as a marker for a poor prognosis. This finding was supported by a study by Lippi et al. (37).

Acute Kidney Injury (AKI) affects approximately 20–40% of COVID-19 patients admitted to intensive care (38). It is considered as a marker of disease severity and a negative prognostic factor for survival (38, 39). AKI can lead to impaired acid-base, fluid, and electrolyte homeostasis, all of which may contribute to worse outcomes for patients with COVID-19 (39). In our cohort the incidence of AKI was 16.2%. A progressive elevation of creatinine was noted as a marker for poor prognosis, yet, only AKI stage 3 was found to be an independent risk factor associated with mortality. AKI is a well-recognised factor of poor prognosis but during the SARS Cov-2 pandemic few studies have found a significant association between AKI and death (38). This might be explained by the findings of Cheng et al. who demonstrated that only AKI Stages 2 or 3 are associated with a high risk of mortality (40).

## Strengths And Limitations

One of the principle weaknesses of this study is that it was carried out in a single centre thus the results cannot be generalised to all COVID-19 patients. Another weakness is that because it is retrospective we were unable to obtain all data related to the parameters of interest. Finally the small sample size was not sufficiently powered to identify potential associations between variables of interest. Nevertheless, this study has the advantage of being the first one in the DRC to examine epidemiological and laboratory data during the course of the admission to evaluate some of the risks of mortality from COVID-19.

## Conclusion

The results from this study demonstrated that an advanced age and raised PCT offered a worse prognosis in COVID-19 patients. In addition, serum levels of C-reactive protein (CRP) and creatinine significantly rose during admission in the non-survivor group compared with those who survived to discharge.

## Abbreviations

AKI: Acute kidney injury; ARDS: acute respiratory distress syndrome ARDS; BOS: Blood oxygen saturation; CK: Creatinin kinase; CKD: chronic kidney disease; CRP: C-reactive protein; CT: computer tomography; Covid-19: Coronavirus disease 2019 ; DRC: democratic republic of Congo; FiO2: inspired oxygen fraction; HB: hemoglobin; HR: heart rate; KMC: Kinshasa medical center; LDH: Lactate dehydrogenase; MV: mechanical ventilation; PaO2: arterial oxygen pressure; PCT: Procalcitonin; PTR: Prothrombin rate; RR: respiratory rate ; RT-PCR: reverse transcriptase polymerase chain reaction; SARS-Cov-2: 2019 novel coronavirus; WBC: white blood cell ; WHO: World Health Organization.

## Declarations

### ***Ethical approval and consent to participate***

This study was carried out in strict compliance with the recommendations of the Declaration of Helsinki III (8). The files were looked was designed anonymously. The information obtained during the history and clinical examination was transcribed into pre-established and pre-coded investigation sheets while respecting the confidentiality and privacy of patients. Our research projects on Covid-19 had been authorized by the National Ethics committee of Health, Democratic Republic of Congo (N°225/CNES/BN/PMMF/2020). Written, informed was waived by the National Ethics committee of Health, Democratic Republic of Congo because of the urgency and unprecedented nature of the COVID-19 pandemic.

## ***Consent for publication***

Not applicable

## ***Availability of data and materiels***

The dataset supporting the conclusion of this article are available

## ***Competing interests***

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be considered as a potential conflict of interest.

## ***Funding***

None

## ***Author contributions***

YN conceived the idea, designed and supervised the study, had full access to all data and took responsibility for the integrity of the data. KVE and JPK were responsible for the diagnosis and treatment of patients. JS, JRN, JA and DB collected the clinical and laboratory data. DM and AN analysed data and performed statistical analysis. All co-authors reviewed and approved the final version.

## **Acknowledgments.**

The authors gratefully thank the staff of the Kinshasa Medical Center (KMC), for their commitment to the provision of excellent care to our patients.

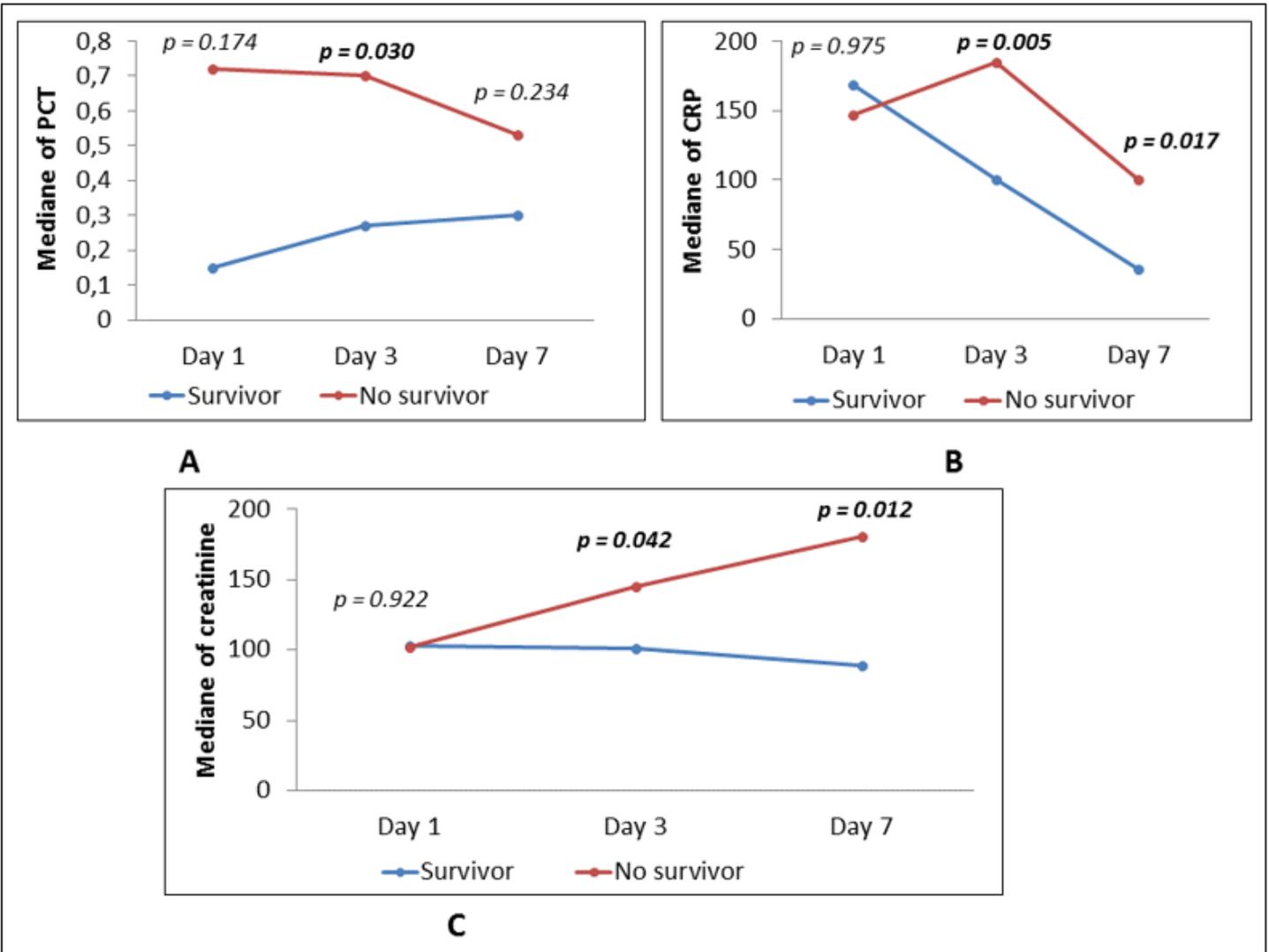
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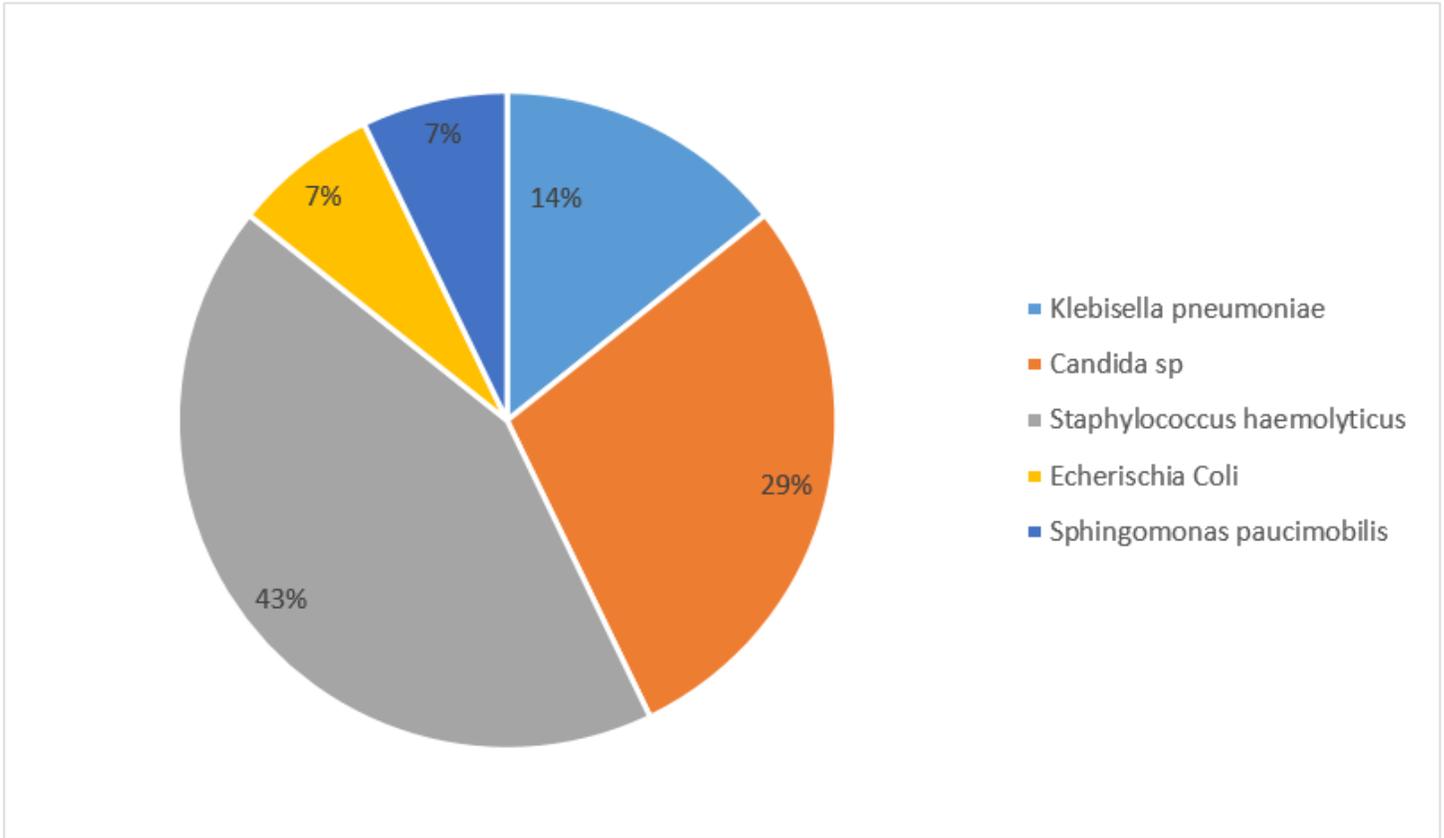
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## Figures



**Figure 1**

Temporal changes in laboratory markers from illness onset in patients hospitalised with COVID-19 Figure shows temporal changes in Procalcitonin (A), C-reactive protein (B) and creatinin (C). Differences between survivors and non-survivors were significant for all timepoints shown



**Figure 2**

Diagram of main secondary infection in COVID-19 patients.

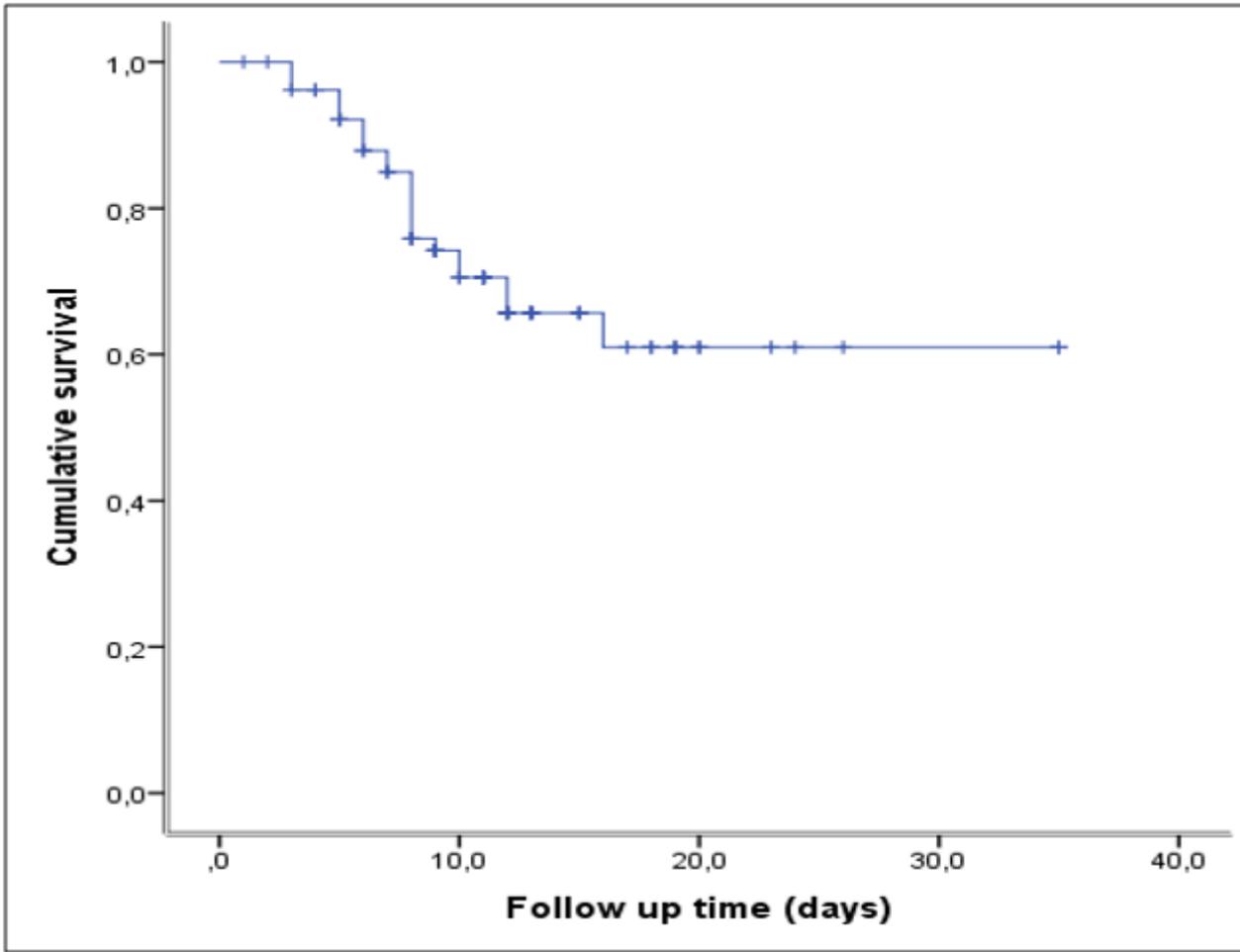
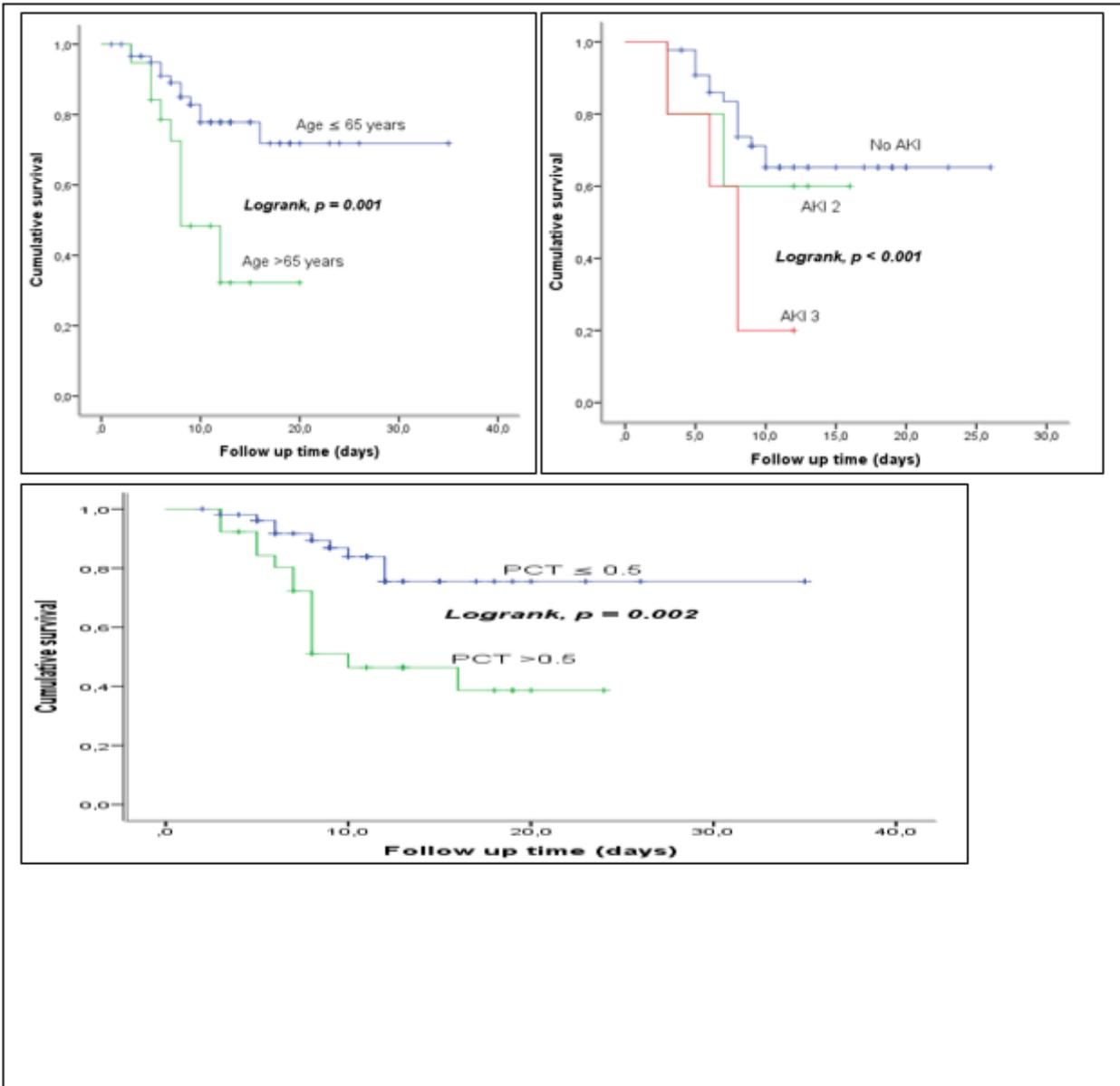


Figure 3

Survival Curve of COVID-19 patients study population.



**Figure 4**

Survival Curves of COVID-19 patients according to Age (A), AKI (B) and procalcitonin (C) status.