

Cardiac arrest and cardiopulmonary resuscitation in hospitalized COVID-19 patients

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has resulted in a marked increase in the incidence of in-hospital cardiac arrest (IHCA), with mortality rates surpassing 90% despite cardiopulmonary resuscitation (CPR) efforts. Patients with COVID-19 who experience IHCA are less likely to present with shockable rhythms, have lower rates of return of spontaneous circulation (ROSC), and exhibit significantly lower survival rates. The aim of this paper was to investigate the epidemiology and clinical features of COVID-19 patients who required CPR following an episode of IHCA.

Study design and methods: Retrospective analysis of adult patients aged 18 years or older, who were admitted to our critical care unit and diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection using reverse transcription polymerase chain reaction (rtPCR) between March 2020 and February 2022. Patients who experienced IHCA at any point during their hospital stay were included in the study. Data were collected for demographics, pre-admission conditions, comorbidities, resuscitation records, severity scores (such as Sequential Organ Failure Assessment [SOFA], Acute Physiology and Chronic Health Evaluation [APACHE] II, and Ichikado CT), laboratory results, length of stay, and survival to hospital discharge.

Results: Nine hundred and ninety-four patients with a COVID-19 diagnosis were admitted to our high-acuity COVID-19 unit during the study period. Out of those, 129 patients underwent CPR. The median age was 63 years old (52-72). Ninety-one (70.5%) patients were male. Sixty-five (50.8%) patients were Hispanic, 34 (26.6%) Caucasian, 22 (17.2%) African American, and 7 (5.5%) other races. The most common comorbidities were systemic arterial hypertension (48.4%) and diabetes mellitus (32%). Thirty-nine patients (30.5%) had no reported comorbidities. The mean APACHE score was 16 (11-23), and the highest APACHE score during hospitalization was 29 (21.5-35). The mean SOFA score was 4 (2-6.5), with the highest SOFA score during hospitalization being 10 (7-13). The mean Ichikado CT score was 200 (150-245) and an Ichikado CT score >174 was present in 68 (63.6%) patients. Twenty-one (16.3%) patients developed pulmonary embolism, 7 (5.4%) patients developed myocarditis, 22 (17.1%) developed acute kidney injury, and 40 (31%) patients developed disseminated intravascular coagulation (DIC). The most frequent cardiac arrest rhythm was asystole (9.8%), followed by pulseless electrical activity (PEA) (2.6%), pulseless ventricular tachycardia (0.5%), and ventricular fibrillation (0.6%). The mean CPR duration was 22.8 minutes. The mortality of patients that underwent CPR was 98.4%.

Conclusions: Most COVID-19 patients who received CPR in this cohort had a severe disease course, with a low survival rate and a short mean survival time. Our findings revealed that male gender, age above 65 years, hospital admission more than 7.5 days after symptom onset, high scores on admission for severity assessment such as APACHE II and SOFA, as well as high levels of creatine phosphokinase (CPK), blood urea nitrogen:creatinine (BUN:Cr) ratio, interleukin 6 (IL-6), and glucose upon admission, and the presence of a cytokine storm at the time of admission were all factors associated with an increased risk of mortality following CPR.

Key words: COVID-19, in-hospital cardiac arrest, severe acute respiratory syndrome, CPR, resuscitation, SARS-CoV-2.

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Introduction

During the pandemic era, there has been a rise in emergency medical services (EMS) utilization, hospitalizations, intensive care unit admissions, and in-hospital mortality rates, surpassing those of other fatal health conditions worldwide. (1,2) Recent studies have revealed that patients with coronavirus disease 2019 (COVID-19) who experienced in-hospital cardiac arrest (IHCA) had considerably lower survival rates when compared to data from the pre-COVID-19 era. (3) Moreover, these patients exhibited a lower proportion of shockable rhythms, lower rates of return of spontaneous circulation (ROSC), and higher mortality rates, which can be as high as 94.9% when compared to 76.7% in non-COVID-19 patients. (4,5) An analysis of COVID-19-related IHCA has revealed in-hospital to 30-day mortality rates of 89.9%, with a high prevalence of non-shockable rhythms at 89%, and a low rate of neurological recovery in survivors at 6%. (3)

A study conducted utilizing data from the Swedish registry of cardiopulmonary resuscitation (CPR) showed that 10% of confirmed COVID-19 cases experienced out-of-hospital cardiac arrest (OHCA) and 16% experienced IHCA, with over 60% of patients presenting with IHCA within 24 hours of hospital admission. (6) Given the high risk of disease transmission and severity associated with COVID-19, the effectiveness of CPR in these patients was of concern. The aim of this study was to analyze the characteristics of COVID-19 patients who underwent IHCA and required CPR and to identify factors that may influence their chances of survival following CPR.

Methods

Study setting and design

A descriptive, retrospective study was conducted in a high-acuity COVID-19 unit. This research was conducted with the approval of our Institutional Review Board and performed according to the ethical standards of the 1964 Declaration of Helsinki.

Patients

The study population was identified using the institution's electronic medical records (EMR) system, Meditech™ (Canton, MA). All adult patients (≥ 18 years old) with a confirmed COVID-19 diagnosis by reverse transcription polymerase chain reaction (rtPCR) who were admitted to the critical care unit between March 2020 and February 2022 were included in the study. Eligible patients were those who experienced in-hospital cardiac arrest (IHCA) at any point during their hospital stay and underwent cardiopulmonary resuscitation (CPR). Patients with

no available resuscitation records were excluded. To eliminate bias and confounding variables that may affect the results of the study, only the first admission to the intensive care unit (ICU) was analyzed.

Data collection

After identifying patients with COVID-19 disease, the inclusion and exclusion criteria were reviewed and the following data were collected: Pre-admission characteristics, demographic information, comorbidities, resuscitation records, severity scores such as Sequential Organ Failure Assessment (SOFA) scores, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, the Ichikado CT score (a lung imaging severity score that was used to assess the severity of lung involvement in the studied patients), laboratory results, length of stay (LOS), and survival to hospital discharge.

In this study, patients who received CPR were compared to both the overall cohort of patients who did not receive CPR, as well as a subgroup of control patients who were matched to the CPR group based on key characteristics (age, gender, and body mass index [BMI]) and selected through random sampling (matched non-CPR group) for a secondary analysis described in **Supplementary Table 1**. A comprehensive, secure database was used to store the data of eligible patients.

Statistical analysis

Data on the characteristics of patients before admission, demographics, and clinical findings were presented using descriptive statistics, multiple logistic regression, Mann-Whitney U-test, chi-square test, and Fisher exact test methods. Continuous variables were summarized as median (interquartile range [IQR]) and percentages. Survival was computed from the date of hospital admission to the date of death before hospital discharge. To determine the OR of the need for CPR and the OR for death, a bivariate logistic regression was conducted using a 2x2 table to identify clinical and demographic confounding factors associated with death. All variables with a p -value < 0.05 were included in a multiple logistic regression model. Significant variables were added one by one until the best predictive model was found that remained statistically significant. Confounding factors for CPR were found to be creatine phosphokinase (CPK) > 91 mg/dl on admission, vasopressin, myocarditis, Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV) infection, while confounding factors for death were identified as interleukin 16 (IL-16) level, Ichikado CT score,

EBV/CMV infection, and sex. Statistical analyses were performed using SPSS 24TM (Armonk, NY), and p-values ≤ 0.05 were considered statistically significant.

Results

Pre-admission characteristics

Nine hundred and ninety-four patients were hospitalized with COVID-19 diagnosis during the study period. Out of those, 129 patients underwent CPR. Compared to the non-CPR group, the CPR group was significantly older, with a median age of 63 years (52-72) vs 55 years (43-66) ($p < 0.001$), had a higher proportion of patients over the age of sixty-five years with 59 (45.7%) patients compared to 234 (27.1%) in the non-CPR group ($p < 0.001$), and had a higher proportion of male patients with 91 (70.5%) patients compared to 468 (54.1%) ($p < 0.001$). The CPR group had 65 (50.8%) Hispanic patients, 34 (26.6%) Caucasians, 22 (17.2%) African American, and 7 (5.5%) of other races. There was no difference in race distribution in the CPR group when compared with the non-CPR group ($p = 0.164$). Hypertension was the most common comorbidity found in 62 (48.4%) cases in the CPR group, followed by type 2 diabetes mellitus in 41 (32%), congestive heart failure in 9 (7%), and peripheral vascular disease in 9 (7%) cases. When compared with the non-CPR group, the CPR group had a higher proportion of individuals with hypertension, 308 (39.4%) vs 62 (48.4%) ($p = 0.004$), congestive heart failure 22 (2.5%) vs 9 (7%) ($p = 0.012$), and peripheral vascular disease 16 (1.9%) vs 9 (7%) ($p = 0.003$). When compared to the matched non-CPR group paired by age, gender, and body mass index (BMI), only hypertension was found to be higher in the CPR group with 62 (48.4%) patients vs 43 (33.3%) patients ($p = 0.019$). Notably, 30.5% of the patient had no reported comorbidities in the CPR group, while 50.8% had no comorbidities in the non-CPR counterpart ($p < 0.001$). This difference was also observed in the matched non-CPR group, where 64 (49.6%) had no reported comorbidities vs 39 (30.5%) in the CPR group ($p = 0.002$) (**Table 1** and **Supplementary Table 1**).

On admission characteristics

The CPR group differed from the matched non-CPR control group in terms of the method of arrival at the hospital. A higher proportion of patients who received CPR were transferred from other hospitals, 38 (29.5%) patients vs 15 (11.7%) patients ($p = 0.003$), whereas a higher proportion of patients who did not receive CPR in the matched group ar-

rived at the hospital by their own means or in an ambulance 96 (75.6%) patients and 10 (7.9%) patients, respectively, or from a long-term care facility or rehabilitation center 6 (4.7%) compared to those that receive CPR with 81 (62.8%), 8 (6.2%), and 2 (1.6%) patients, respectively, ($p = 0.003$). Bivariate analysis showed that being transferred from another institution was associated with a higher likelihood of requiring CPR, with an odd ratio of 2.61 (95% CI: 1.34-5.09, $p = 0.005$), while arriving at the hospital by one's own means was associated with a lower likelihood of receiving CPR, with an odd ratio of 0.53 (95% CI: 0.31-0.91, $p = 0.022$). This suggests that arriving by one's own means may be a protective factor against receiving CPR (**Supplementary Table 3**). The time from symptom onset to admission was significantly longer in the CPR group, 7 (4-10) days, compared to the group that did not receive CPR, 6 (3-8) days ($p = 0.007$) (**Supplementary Table 1**).

The mean APACHE II score on admission was higher in the CPR group compared to the non-CPR group, 16 (11-23) vs 8 (5-12), ($p < 0.001$). A similar trend was seen when comparing the CPR group with an APACHE II score of 16 (11-23) to the matched non-CPR control group with 7 (4.5-12) ($p < 0.001$). Similarly, the mean SOFA score on admission in the CPR group was statistically higher when compared to those in the non-CPR, 4 (2-6.5) vs 2 (1-3) ($p < 0.001$). This trend was maintained for admission SOFA score when comparing the CPR group with the matched non-CPR control group, 4 (2-6.5) vs 2 (1-4) ($p < 0.001$). The Ichikado CT score was significantly higher, with 200 (150-245) in the CPR group vs 140 (120-190) in the non-CPR population ($p < 0.001$), and Ichikado CT score > 174 was present in 68 (63.6%) patients in the CPR group vs 251 (32.7%) patients in the non-CPR group ($p < 0.001$). The same pattern was found when analyzing the matched non-CPR group, showing lower admission Ichikado CT score of 150 (120-200) compared to 200 (150-245) in the CPR group ($p < 0.001$) (**Table 2** and **Supplementary Table 2**).

Upon admission, a significantly higher proportion of patients in the CPR group had CPK > 91 mg/dl when compared to the non-CPR group, 124 (95.9%) patients vs 495 (60.1%) patients, respectively ($p < 0.001$). In addition, there was a higher number of individuals with BUN/Cr ≥ 20 in the CPR group when compared to the non-CPR group, 77 (60.2%) patients vs 343 (39.9%) patients ($p = 0.001$). Similar results were obtained when comparing the CPR group with the matched non-CPR group, with a higher proportion of patients in the CPR group having CPK levels > 91 mg/dl (95.9% vs 76.2%,

$p < 0.001$) and BUN/Cr ≥ 20 (60.2% vs 44.2%, $p = 0.015$) (**Supplementary Table 2**).

In the CPR group, the absolute CD4⁺ value was found to be significantly lower compared to the non-CPR group upon admission (225 [145-375] cells/ μ l vs 336 [200-539] cells/ μ l, respectively, $p < 0.001$). Furthermore, the proportion of patients with CD4⁺ values < 200 was higher in the CPR group (18.9%) compared to the non-CPR group (8.5%) with statistical significance ($p = 0.003$). Similarly, patients who received CPR had a lower CD8⁺ cell count than those who did not (121 [77-214] cells/ μ l vs 194 [117-344] cells/ μ l, respectively, $p < 0.001$). Additionally, a significantly higher proportion of patients in the CPR group had CD8⁺ cell counts < 100 cells/ μ l compared to the non-CPR group (75.5% vs 37.2%, respectively, $p < 0.001$) (**Table 1**). In the CPR group, both IL-6 and IL-10 levels were significantly higher compared to the non-CPR group. The IL-6 values were 27 (9.8-77.5) pg/ml vs 7.6 (2.7-24.9) pg/ml ($p < 0.001$), and the IL-10 values were 24 (12-44.6) pg/ml vs 12.9 (7.9-21.6) pg/ml ($p < 0.001$) (**Table 1**). When comparing the CPR group with the matched non-CPR control group, the first recorded CD4⁺ cell count was not significantly different ($p = 0.117$), while the CD8⁺ count was significantly lower in the CPR group (121 [77-214] cells/ μ l) compared to the matched non-CPR control group (173 [90-239.5] cells/ μ l) ($p = 0.035$). Similarly, IL-6 and IL-10 levels were significantly higher in the CPR group than in the matched non-CPR control group. The IL-6 values were 27 (9.8-77.5) pg/ml vs 7.6 (3.2-24.6) pg/ml ($p < 0.001$), while the IL-10 values were 24 (12-44.6) pg/ml vs 12.6 (8.9-24.1) pg/ml ($p < 0.001$).

During hospitalization

EBV infection was present in 46 (56.8%) patients in the CPR group vs 125 (34.2%) patients in the non-CPR group, ($p < 0.001$). EBV and CMV coinfection was observed in 60 (74.1%) patients who underwent CPR and 156 (42.7%) patients in the non-CPR group ($p < 0.001$). No significant difference was noted with regards to CMV infection between the CPR group and non-CPR group, 6 (7.4%) vs 12 (3.3%) ($p = 0.113$). Candida infection was found in greater proportion in the CPR group, compared to the non-CPR group, 12 (11.3%) vs 27 (4.1%) ($p = 0.004$). Staphylococcus spp infection was observed to be present in a higher proportion in the CPR group compared to the non-CPR group, with 28 (26.2%) cases vs 82 (12.5%) cases ($p < 0.001$). An increased proportion of EBV infection was seen in the CPR group when compared with the matched non-CPR group, with 73 (56.8%) cases vs 21

(36.2%) cases ($p = 0.026$). EBV and CMV infections were also found to be higher in the CPR group compared to the matched non-CPR group, with 60 (74.1%) cases vs 27 (46.6%) cases ($p < 0.001$). Staphylococcus spp was found in higher proportion in the CPR group compared to the matched non-CPR group 28 (26.2%) cases vs 13 (13.5%) cases ($p = 0.039$). The ratio of CD4⁺ cell count on admission to lowest CD4⁺ cell count during hospital stay was significantly higher in the CPR group compared to the non-CPR group being 1.70 (1.03-3.87) vs 1.15 (1.00-2.35), respectively ($p < 0.001$). Similarly, the ratio of CD8⁺ cell count on admission to lowest CD8⁺ cell count during hospitalization was significantly higher in the CPR group vs non-CPR group, being 1.72 (1.00-3.64) vs 1.16 (1.09-1.97) ($p < 0.001$) (**Table 2** and **Supplementary Table 2**). During the hospital course, patients that needed CPR developed more complications. Twenty-one (16.3%) patients in the CPR group vs 51 (5.9%) in the non-CPR group, developed pulmonary embolism ($p < 0.001$), 7 (5.4%) patients in the CPR group had myocarditis when compared to 6 (0.7%) in the non-CPR group ($p < 0.001$), 22 (17.1%) patients in the CPR group developed acute kidney injury compared to 58 (6.7%) in the non-CPR group ($p < 0.001$), and 40 (31%) patients in the CPR group developed disseminated intravascular coagulation (DIC) when compared to 117 (13.5%) in the non-CPR group ($p < 0.001$). Length of stay was higher in the CPR group, 7 (4-12) days vs 6 (4-11) days in the non-CPR ($p < 0.001$).

Bivariate and multivariate analyses were performed to determine the factors associated with death and CPR. Multiple logistic regression revealed that CPK > 91 mg/dl on admission (aOR: 26.04, 95% CI: 2.0-337.1), use of vasopressin (aOR: 9.3, 95% CI: 2.9-30.4), myocarditis during hospitalization (aOR: 9.1, 95% CI: 1.4-60.7), EBV and/or CMV infection (aOR: 3.8, 95% CI: 1.4-10.4) were all factors associated with a higher risk of death in patients that received CPR (**Table 3**). In multivariate logistic regression, undergoing CPR (aOR: 3,325.4, 95% CI: 143.4-77119.4), IL-6 > 12 pg/ml on admission (aOR: 21.2, 95% CI: 5.6-76.01), Ichikado > 174 on admission (aOR: 7.9, 95% CI: 2.4-26.2), EBV and/or CMV infection (aOR: 6.9, 95% CI: 2.1-22.1), age > 65 years (aOR: 6.0, 95% CI: 2.1-172), and male gender (aOR: 4.5, 95% CI: 1.4-15.6) were the best predictors for increased likelihood of death in COVID-19 patients (**Table 4**).

CPR characteristics

Of the 129 patients who received CPR, the median age was 65 years old (52-72 years). Ninety-one

(70.5%) of these patients were male and 38 (29.5%) were female. The time from admission to CPR was 12 days (6-18.5 days). The duration of CPR for these patients was 20 minutes (13.75-29 minutes). Two patients (1.6%) had ventricular fibrillation, five (3.9%) had pulseless ventricular tachycardia, 25 (19.2%) had pulseless electrical activity, and 97 (75.2%) had asystole as the resuscitation rhythm. Out of the 129 patients, only two (1.6%) survived hospital discharge. Both patients had asystole during resuscitation, and on a 6-month follow-up, both patients remained alive and neurologically intact. Finally, 187 (18.1%) patients in the non-CPR group died during the study period vs 127 (98.4%) patients that died in the CPR group.

Discussion

Previous studies have shown that COVID-19 patients who suffered from IHCA or OHCA had a lower survival rate and a higher prevalence of non-shockable rhythms compared to non-COVID-19 patients. (3,7) However, the data regarding OHCA is still debated, as some studies have found that there was no difference in the rates of ROSC, neurological outcomes, or survival rates for OHCA patients before and after the COVID-19 pandemic. (8) Our study shows that most COVID-19 patients who had IHCA needing CPR had a relatively more severe disease course, with a survival rate of 1.6% and a mean survival time of 12 days compared to those that did not need CPR.

Our analysis showed that the male gender was an independent risk factor that increased the risk of death following CPR by approximately 6 times, and that age older than 65 years old increased the risk of death by a factor of approximately 7. More importantly, our study revealed that patients arriving at the hospital on their own means, as opposed to being transferred from a different hospital, had a lower risk of experiencing IHCA and requiring CPR later during their hospitalization. In contrast, patients that were transferred from different hospitals required CPR 69% of the time. However, all patients that presented to our hospital later than 7.5 days after symptom onset, had a more severe hospital course and were more likely to develop IHCA requiring CPR.

The accuracy of the APACHE II and SOFA scores in predicting mortality among COVID-19 patients is still uncertain. Our study showed that an APACHE II score of more than 15 and a SOFA score greater than 2 upon admission were the most reliable predictors of IHCA requiring CPR in COVID-19 patients. Furthermore, our findings revealed that a higher Ichikado CT score was ob-

served in patients who underwent CPR compared to those who did not require CPR and the matched control group. Notably, an Ichikado CT score greater than 174 was present in a substantial number of COVID-19 patients who needed CPR and it was linked to an increased risk of death.

Abderrahim and coinvestigators have previously reported that there was no association between biochemical parameters on admission and COVID-19-related mortality. (9) However, our observations were different. Several biochemical parameters were identified on admission that significantly impacted the likelihood of death following CPR in COVID-19 patients (such as CPK>91 mg/dl, BUN:Cr \geq 20, IL-6>12 pg/ml). Furthermore, we also found evidence of a dysfunctional immune response early in the disease process, increasing mortality as we observed significantly higher white blood cell (WBC) count on admission in patients that eventually developed IHCA needing CPR with a significantly elevated neutrophil count, a significantly reduced lymphocyte and platelet count showing signs of NETosis. These findings have been described before by Liu and coinvestigators, who noted that 80% of COVID-19 patients had normal or decreased WBC counts, and 72.3% had lymphopenia. (10) Similarly, Bin Zhu and coinvestigators described that COVID-19 patients with higher WBC counts had an increased risk for death. (11)

Our study highlights the significance of EBV and CMV infections during hospital stays, as they were found to be strongly associated with increased mortality risk among COVID-19 patients who underwent CPR. Patients infected with both viruses had a 3.8-fold higher risk of post-CPR death and an 8.7-fold higher risk of death during the COVID-19 disease process. Interestingly, EBV infection alone had a slightly weaker association with IHCA and CPR requirements when compared to cases with both viruses present. Conversely, CMV infection alone had an even weaker association with IHCA than EBV infection alone. Infections with Staphylococcus and Candida were also significantly associated with IHCA, but to a lesser extent when compared to combined EBV-CMV infection.

Previous studies have shown that cytotoxic immunity plays a key role in combating viral infections and can influence the severity of the disease and the likelihood of recovery. (12-15) COVID-19 has been linked to a reduction in the number of circulating lymphocytes, specifically CD4⁺ and CD8⁺ cells, which can lead to reinfection with viruses such as EBV and CMV. (16) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has also been shown to cause lymphopenia by several mecha-

nisms, including T-lymphocyte apoptosis resulting in a transient reduction in the number of circulating lymphocytes, particularly in patients with moderate or severe cases of the disease. (16) In this study, we found that patients who required CPR due to COVID-19 had a 70% reduction in CD4⁺ cell count, and a 72% reduction in CD8⁺ cells from admission as compared to those who did not need CPR, highlighting the role of lymphocytes in determining the severity of the COVID-19 illness.

Our study found that DIC, myocarditis, and pulmonary embolism were all adverse events that can occur in COVID-19 patients during their hospitalization and significantly increase the risk of IHCA requiring CPR. In fact, myocarditis was found to be a particularly high-risk factor, as it increased the risk of death after CPR by 9 times.

The findings of our research underscore the significance of recognizing the particular traits that could potentially result in IHCA among patients diagnosed with COVID-19. In particular, COVID-19 patients who are older males with more severe biochemical levels may be at an increased risk of experiencing IHCA. The goal was to provide clinicians with the tools and knowledge necessary to deliver optimal care to patients with COVID-19 and reduce the incidence of adverse events such as IHCA and thus improve outcomes, especially after implementing CPR.

The accuracy and completeness of the medical records used in the present retrospective cohort study were subject to potential sources of bias, such as human error during data entry. It should be considered that the quality of the records can vary depending on who entered the information, which may impact the interpretation of the study findings. Secondly, the study was conducted in an intensive care unit that did not have access to certain supportive therapies, such as extracorporeal membrane oxygenation (ECMO), which could impact patient outcomes.

Thirdly, it should be noted that the exact timing from cardiac arrest to CPR maneuvers was not registered in our study, although all patients were in the intensive care unit, and best practice protocols were strictly followed to minimize any potential impact on patient outcomes. Lastly, information on vaccination status for the population studied was not available for analysis, precluding any conclusions about the potential effect of vaccines on disease severity and outcomes.

Conclusions

COVID-19 patients who experienced IHCA and received CPR tended to have a more severe disease course with low survival rates and short mean survival times. Our study identified several risk factors for death following CPR in COVID-19 patients, including male gender, age over 65, late presentation to the hospital (>7.5 days after symptom onset), transfer from another hospital, an APACHE II score >15, SOFA score >2, and an Ichikado CT score >174. Furthermore, admission biochemical markers and a significant decrease in CD4⁺ and CD8⁺ cell counts leading to opportunistic infections during hospitalization were also associated with a higher risk of IHCA and death. Future research should continue to explore the effectiveness of CPR in COVID-19 patients and identify additional factors that may influence its effectiveness and improve outcomes.

Conflicts of interest

The authors have no conflict of interest in the preparation of this manuscript. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

*This article was presented as a poster presentation at the Resuscitation Science Symposium of the American Heart Association in November 2022.

Table 1. Demographic data of patients hospitalized due to COVID-19 and cardiopulmonary resuscitation

	All	No CPR	CPR	p
n	994	865 (87.0%)	129 (13.0%)	
Age* ⁺	56 (44-67)	55 (43-66)	63 (52-72)	<0.001
Age >65 years	293 (29.5%)	234 (27.1%)	59 (45.7%)	<0.001
Sex ^{&}				
- Male	559 (56.2%)	468 (54.1%)	91 (70.5%)	<0.001
- Female	435 (43.8%)	397 (45.9%)	38 (29.5%)	
Race ^{&}				
- Caucasian	196 (20.0%)	162 (19.0%)	34 (26.6%)	0.164
- Hispanic	538 (54.9%)	473 (55.5%)	65 (50.8%)	
- African American**	206 (21.0%)	184 (21.6%)	22 (17.2%)	
- Other	40 (4.1%)	33 (3.9%)	7 (5.5%)	
BMI* ⁺	29.3 (25.8-34.5)	29.4 (25.8-34.5)	29.1 (25.8-35.7)	0.919
Comorbidities				
- Systemic arterial hypertension ^{&}	368 (37.1%)	306 (35.4%)	62 (48.4%)	0.004
- Diabetes mellitus ^{&}	251 (25.3%)	210 (24.3%)	41 (32.0%)	0.077
- COPD ^{&}	28 (2.8%)	22 (2.5%)	6 (4.7%)	0.161
- Previous myocardial infarction ^{&}	19 (1.9%)	15 (1.7%)	4 (3.1%)	0.293
- Congestive heart failure [#]	31 (3.1%)	22 (2.5%)	9 (7.0%)	0.012
- Chronic kidney disease [#]	26 (2.6%)	23 (2.7%)	3 (2.3%)	1.000
- Peripheral vascular disease ^{&}	25 (2.5%)	16 (1.9%)	9 (7.0%)	0.003
- Stroke/TIA [#]	23 (2.3%)	18 (2.1%)	5 (3.9%)	0.205
- Dementia [#]	15 (1.5%)	13 (1.5%)	2 (2.6%)	1.000
- Connective tissue disease [#]	11 (1.1%)	8 (0.9%)	3 (2.3%)	0.160
- Peptic ulcer disease [#]	16 (1.6%)	4 (0.5%)	12 (9.4%)	<0.001
- Liver disease [#]	14 (1.4%)	11 (1.3%)	3 (2.3%)	0.409
- Hemiplegia [#]	4 (0.4%)	1 (0.1%)	2 (2.3%)	0.008
- Solid tumor [#]	11 (1.1%)	7 (0.8%)	4 (3.1%)	0.042
- Leukemia [#]	3 (0.3%)	3 (0.3%)	0 (0.0%)	1.000
- Lymphoma [#]	2 (0.2%)	2 (0.2%)	0 (0.0%)	1.000
- Other comorbidities ^{&}	374 (37.7%)	320 (37.0%)	54 (42.2%)	0.306
- No comorbidities ^{&}	478 (48.2%)	439 (50.8%)	39 (30.5%)	<0.001

Legend: COVID-19=coronavirus disease 2019; CPR=cardiopulmonary resuscitation; BMI=body mass index; COPD=chronic obstructive pulmonary disease; TIA=transient ischemic attack.

*Median (p25-p75), ⁺Mann-Whitney U-test, [&]Chi-square test, **Chi-square test <0.001, [#]Fisher exact test.

Table 2. Clinical, biochemical, immunological, and infectious risk factors for CPR

	All	No CPR	CPR	p
n	994	865 (87.0%)	129 (13.0%)	
Severity scores				
- APACHE score* ⁺	9 (6-13)	8 (5-12)	16 (11-23)	<0.001
- APACHE score >15 on admission ^{&}	167 (16.8%)	99 (11.5%)	68 (52.7%)	<0.001
- Highest APACHE score* ⁺	10 (7-17)	9 (6-14)	29 (21.5-35)	<0.001
- SOFA score* ⁺	2 (1-3)	2 (1-3)	4 (2-6.5)	<0.001
- SOFA score >2 on admission ^{&}	318 (32.1%)	223 (25.8%)	95 (73.6%)	<0.001
- Highest SOFA score* ⁺	2 (2-5)	2 (1-4)	10 (7-13)	<0.001
- Ichikado score* ⁺	150 (120-200)	140 (120-190)	200 (150-245)	<0.001
- Ichikado score >174 ^{&}	319 (36.5%)	251 (32.7%)	68 (63.6%)	<0.001
Mechanical ventilation	159 (16.0%)	138 (16.0%)	21 (16.3%)	1.000
Biochemical parameters				
- Na level on admission* ⁺	136 (133-138)	136 (133-138)	135 (132-138)	0.209
- K level on admission* ⁺	3.9 (3.6-4.3)	3.9 (3.6-4.2)	4.0 (3.7-4.4)	0.019
- Cl level on admission* ⁺	101 (98-104)	101 (98-104)	100 (97-104)	0.470
- HCO ₃ level on admission* ⁺	24 (22-27)	24 (22-27)	23 (21-26)	0.082
- BUN level on admission* ⁺	14 (10-21)	13 (10-20)	21 (14-37)	<0.001
- Cr level on admission* ⁺	0.8 (0.6-1.1)	0.8 (0.6-1.0)	0.9 (0.7-1.2)	<0.001
- Glucose level on admission* ⁺	120 (101-159)	117 (100-151)	141 (113-208.5)	<0.001
- CPK highest value	89 (46-209.8)	84 (46-191.8)	133 (53.8-347.3)	<0.001
- CPK >91 mg/dl during admission	619 (65.1%)	495 (60.1%)	124 (96.9%)	<0.001
- BUN/Cr on admission	17.8 (13.3-24.1)	17.2 (13.3-23.3)	22.5 (16.0-33.6)	<0.001
- BUN/Cr on admission ≥20	421 (42.6%)	343 (39.9%)	78 (60.5%)	<0.001
Immunological parameters				
- WBC level on admission* ⁺	7.1 (5.2-10.2)	6.9 (5.1-9.8)	8.8 (5.8-14.2)	0.008
- Neutrophil level on admission* ⁺	5.4 (3.6-8.4)	5.3 (3.5-7.9)	7.1 (4.5-12.7)	0.008
- Lymphocyte level on admission* ⁺	0.9 (9.6-1.3)	1.0 (0.6-1.4)	0.8 (0.5-1.1)	0.008
- Monocyte level on admission* ⁺	0.5 (0.3-0.7)	0.5 (0.3-0.8)	0.3 (0.1-0.6)	0.437
- Platelets on admission	218 (163-285)	219 (166.3-288)	199 (149-269)	0.043
- ESR level on admission	60 (32-92)	58 (30-90)	73.5 (40-97.8)	0.008
- PT on admission	11 (10.6-11.7)	11 (10.5-11.7)	11.4 (10.7-12)	0.003
- aPTT on admission	29 (27-32)	29 (27-32)	31 (27-34)	0.017
- D-dimer level on admission	0.45 (0.26-1.00)	0.42 (0.24-0.90)	0.68 (0.38-1.72)	<0.001
- CD4 ⁺ first recorded value* ⁺	315 (192-516)	336 (200-539)	225 (145-375)	<0.001
- CD4 ⁺ T cells <200 cells/ml on admission ^{&}	77 (9.9%)	57 (8.5%)	20 (18.2%)	0.003
- CD8 ⁺ first recorded value* ⁺	185 (108-323)	194 (117-344)	121 (77-214)	<0.001
- CD8 ⁺ T-cells <100 cells/ml on admission ^{&}	332 (42.6%)	249 (37.2%)	83 (75.5%)	<0.001
- First recorded CD4 ⁺ /CD8 ⁺ ratio* ⁺	1.72 (1.13-2.69)	1.67 (1.26-2.54)	2.08 (1.26-2.98)	0.016
- CD4 ⁺ on admission/CD4 ⁺ lower value	1.23 (1.00-2.45)	1.15 (1.0-2.35)	1.70 (1.03-3.87)	<0.001
- CD8 ⁺ on admission/CD8 ⁺ lower value	1.23 (1.0-2.09)	1.16 (1.09-1.97)	1.72 (1.00-3.64)	<0.001
- IL-6 first recorded value* ⁺	9.1 (3.1-31.3)	7.6 (2.7-24.9)	27 (9.8-77.5)	<0.001
- IL-6 first recorded >12 pg/ml ^{&}	358 (44.0%)	277 (39.5%)	81 (72.3%)	<0.001
- IL-10 first recorded value* ⁺	13.5 (8.2-24.0)	12.9 (7.9-21.6)	24 (12.0-44.6)	<0.001
- IL-10 first recorded >35 pg/ml ^{&}	102 (14.8%)	67 (11.4%)	35 (35.7%)	<0.001

Other infections				
- EBV infection/reactivation ^{&}	171 (38.3%)	125 (34.2%)	46 (56.8%)	<0.001
- CMV infection/reactivation ^{&}	18 (4.0%)	12 (3.3%)	6 (7.4%)	0.113
- EBV and CMV infection or reactivation ^{&}	216 (48.4%)	156 (42.7%)	60 (74.1%)	<0.001
- Candida infection ^{&}	39 (5.1%)	27 (4.1%)	12 (11.3%)	0.004
- Staphylococcus infection ^{&}	110 (14.4%)	82 (12.5%)	28 (26.2%)	<0.001
Pulmonary embolism (adverse effect or complication) ^{&}	72 (7.2%)	51 (5.9%)	21 (16.3%)	<0.001
Myocarditis (adverse effect or complication) [#]	13 (1.3%)	6 (0.7%)	7 (5.4%)	<0.001
Acute kidney injury (adverse effect or complication) ^{&}	80 (8.0%)	58 (6.7%)	22 (17.1%)	<0.001
Liver failure (adverse effect or complication) [#]	26 (2.6%)	18 (2.1%)	8 (6.2%)	0.013
Gastrointestinal bleeding (adverse effect or complication) [#]	9 (0.9%)	4 (0.5%)	5 (3.9%)	0.003
Hematology-DIC (adverse effect or complication) ^{&}	157 (15.8%)	117 (13.5%)	40 (31.0%)	<0.001
Days hospitalized ^{*+}	7 (4-12)	6 (4-11)	12 (6-18.5)	<0.001
Length of hospitalization >12 days	235 (23.6%)	173 (20.0%)	62 (48.1%)	<0.001
Death ^{&}	187 (18.8%)	60 (6.9%)	127 (98.4%)	<0.001

Legend: CPR=cardiopulmonary resuscitation; APACHE=Acute Physiology and Chronic Health Evaluation; SOFA=Sequential Organ Failure Assessment; Na=sodium; K=potassium; Cl=chloride; HCO₃=bicarbonate; BUN=blood urea nitrogen; Cr=creatinine; CPK=creatine phosphokinase; WBC=white blood cell; ESR=erythrocyte sedimentation rate; PT=prothrombin time; aPTT=activated partial thromboplastin time; IL-6=interleukin 6; IL-10=interleukin 10; EBV=Epstein-Barr virus; CMV=cytomegalovirus; DIC=disseminated intravascular coagulation.

*Median (p25-p75), ⁺Mann-Whitney U-test, [&]Chi-square test, [#]Fisher exact test.

Table 3. Bivariate and multiple analyses to determine COVID-19 death risk factors for CPR

Factors	All	No CPR	CPR	RR crude	RR adjusted*
CPK>91 mg/dl on admission	619 (65.1%)	495 (60.1%)	124 (96.9%)	20.5 (7.5-56.1, p<0.001)	26.04 (2.0-337.1, p=0.013)
Use of vasopressin	55 (5.6%)	19 (2.2%)	36 (27.9%)	17.1 (9.4-31.1, p<0.001)	9.3 (2.9-30.4, p<0.001)
Myocarditis during hospitalization	13 (1.3%)	7 (9.7%)	13 (1.3%)	8.2 (2.7-24.9, p<0.001)	9.1 (1.4-60.7, p=0.022)
EBV and/or CMV infection	216 (48.4%)	156 (42.7%)	60 (74.1%)	3.8 (2.2-6.6, p<0.001)	3.8 (1.4-10.4, p=0.010)
BUN/Cr ratio≥20 on admission	421 (42.6%)	343 (39.9%)	78 (60.5%)	2.3 (1.6-3.4, p<0.001)	2.8 (1.1-7.0, p=0.32)

Legend: COVID-19=coronavirus disease 2019; CPR=cardiopulmonary resuscitation; RR=relative risk; CPK=creatinine phosphokinase; EBV=Epstein-Barr virus; CMV=cytomegalovirus; BUN=blood urea nitrogen; Cr=creatinine.

*Multiple logistic regression, this model can explain 86.9% of the deaths. Intersection B=-7.354, sig<0.001.

Table 4. Bivariate and multiple analyses to determine COVID-19 death risk factors

Factors	All	Survive	Death	RR crude	RR adjusted*
CPR performed	129 (13.0%)	2 (0.2%)	127 (67.9%)	852.0 (205.7-3,528.7, p<0.001)	3,325.4 (143.4-77,119.4, p<0.001)
IL-6>12 pg/ml on admission	358 (44.0%)	232 (35.9%)	126 (75.9%)	5.6 (3.8-8.3, p<0.001)	21.2 (5.9-76.01, p<0.001)
Ichikado CT>174 on admission	319 (36.5%)	215 (29.9%)	104 (67.1%)	4.8 (3.3-6.9, p<0.001)	7.9 (2.4-26.2, p<0.001)
EBV and/or CMV infection	216 (48.4%)	130 (39.6%)	86 (72.9%)	4.1 (2.6-6.5, p<0.001)	6.9 (2.1-22.1, p=0.001)
Age >65 years	293 (29.5%)	199 (24.7%)	94 (50.3%)	3.1 (2.2-4.3, p<0.001)	6.0 (2.1-17.2, p<0.001)
Male	559 (56.2%)	429 (53.2%)	130 (69.5%)	2.0 (1.4-2.9, p<0.001)	4.5 (1.4-15.6, p=0.011)

Legend: COVID-19=coronavirus disease 2019; RR=relative risk; CPR=cardiopulmonary resuscitation; IL-6=interleukin 6; CT=computerized tomography; EBV=Epstein-Barr virus; CMV=cytomegalovirus.

*Multiple logistic regression, this model can explain 91.4% of the deaths. Intersection B=-30.734, sig<0.001.

Supplementary Table 1. Demographic data of patients hospitalized due to COVID-19 and CPR (matched non-CPR group analysis)

	All	Matched non-CPR	Case	p
n	258	129	129	
Age*	61.5 (52-71)	61 (52-71)	62 (52-72)	0.669
Age>65 years	110 (43.0%)	52 (40.3%)	59 (45.7%)	0.451
Sex ^{&}				
- Male	182 (70.5%)	91 (70.5%)	91 (70.5%)	1.000
- Female	76 (29.5%)	38 (29.5%)	38 (29.5%)	
Race ^{&}				
- Caucasian	59 (23.0%)	25 (19.4%)	34 (26.6%)	0.450
- Hispanic	132 (51.4%)	67 (51.9%)	65 (50.8%)	
- African American**	52 (20.2%)	30 (23.3%)	22 (17.2%)	
- Other	14 (5.4%)	7 (5.4%)	7 (5.5%)	
BMI* ⁺	28.8 (25.8-33.7)	28.4 (25.9-32.7)	29.1 (25.8-35.7)	0.608
Comorbidities				
- Systemic arterial hypertension ^{&}	105 (40.9%)	43 (33.3%)	62 (48.4%)	0.019
- Diabetes mellitus ^{&}	78 (30.4%)	37 (28.7%)	41 (32.0%)	0.654
- COPD [#]	10 (3.9%)	4 (3.1%)	6 (4.7%)	0.540
- Previous myocardial infarction [#]	8 (3.1%)	4 (3.1%)	4 (3.1%)	1.000
- Congestive heart failure [#]	13 (5.1%)	4 (3.1%)	9 (7.0%)	0.249
- Chronic kidney disease [#]	7 (2.7%)	4 (3.1%)	3 (2.3%)	1.000
- Peripheral vascular disease ^{&}	13 (5.15)	4 (3.1%)	9 (7.0%)	0.249
- Stroke/TIA [#]	8 (3.1%)	3 (2.3%)	5 (3.9%)	0.500
- Dementia [#]	7 (2.7%)	5 (3.9%)	2 (1.6%)	0.477
- Connective tissue disease [#]	4 (1.6%)	1 (0.8%)	3 (2.3%)	0.370
- Peptic ulcer disease ^{&}	13 (5.1%)	1 (0.8%)	12 (9.4%)	0.004
- Liver disease [#]	6 (2.3%)	3 (2.3%)	3 (2.3%)	1.000
- Hemiplegia [#]	3 (1.2%)	0 (0.0%)	3 (2.3%)	0.122
- Solid tumor [#]	5 (1.9%)	1 (0.8%)	4 (3.1%)	0.231
- Other comorbidities ^{&}	100 (38.9%)	46 (35.7%)	54 (42.2%)	0.344
- No comorbidities ^{&}	103 (40.1%)	64 (49.6%)	39 (30.5%)	0.002
COVID-19 vaccination	14 (6.5%)	6 (5.0%)	8 (8.2%)	0.513
Days between onset of symptoms and admission	7 (4-10)	6 (3-8)	7 (4.3-12.5)	0.007

Legend: COVID-19=coronavirus disease 2019; CPR=cardiopulmonary resuscitation; BMI=body mass index; COPD=chronic obstructive pulmonary disease; TIA=transient ischemic attack.

*Median (p25-p75), ⁺Mann-Whitney U-test, [&]Chi-square test, [#]Fisher exact test, **Chi-square test<0.001.

Supplementary Table 2. Clinical, biochemical, immunological, and infectious risk factors for CPR (matched non-CPR group analysis)

	All	Matched non-CPR	CPR	p
n	258	129	129	
Severity scores				
- APACHE score* ⁺	12 (7.8-19)	7 (4.5-12)	16 (11-23)	<0.001
- APACHE score >15 on admission ^{&}	90 (34.9%)	22 (17.1%)	68 (52.7%)	<0.001
- Highest APACHE score* ⁺	19 (10-32)	11 (7-17)	29 (21.5-35)	<0.001
- SOFA score* ⁺	3 (2-5)	2 (1-4)	4 (2-6.5)	<0.001
- SOFA score >2 on admission ^{&}	141 (54.7%)	46 (35.7%)	95 (73.6%)	<0.001
- Highest SOFA score* ⁺	6 (2-11)	3 (2-4.5)	10 (6-13)	<0.001
- Ichikado score* ⁺	170 (130-225)	150 (120-200)	200 (150-245)	<0.001
- Ichikado score >174 ^{&}	112 (49.8%)	44 (37.3%)	68 (63.6%)	<0.001
Biochemical parameters				
- Na level on admission* ⁺	135 (133-138)	136 (133-138)	135 (132-138)	0.267
- K level on admission* ⁺	4.0 (3.7-4.3)	4 (3.7-4.3)	4 (3.7-4.4)	0.430
- Cl level on admission* ⁺	100 (97-104)	100 (97.5-104)	100 (97-104)	0.646
- HCO ₃ level on admission* ⁺	24 (22-26)	24 (22-27)	23 (21-26)	0.259
- BUN level on admission* ⁺	18 (12-32)	15 (12-24)	21 (14-37)	<0.001
- Cr level on admission* ⁺	0.9 (0.7-1.2)	0.9 (0.7-1.2)	0.9 (0.7-1.2)	0.378
- Glucose level on admission* ⁺	128 (106.8-177.5)	116 (99-151.5)	141 (113-208.5)	<0.001
- CPK highest value	128.5 (53.8-284.3)	115.5 (53.8-250.5)	133 (53.8-347.3)	0.164
- CPK >91 mg/dl during admission	220 (86.6%)	96 (76.2%)	124 (95.9%)	<0.001
- BUN/Cr on admission	20.0 (14.3-27.7)	17.8 (13.3-25.0)	22.5 (16.0-33.6)	<0.001
- BUN/Cr on admission ≥20 ^{&}	134 (52.1%)	57 (44.2%)	78 (60.5%)	0.015
Immunological parameters				
- WBC level on admission* ⁺	7.7 (5.4-11.8)	7.2 (5.1-9.4)	8.8 (5.8-14.2)	<0.001
- Neutrophil level on admission* ⁺	5.9 (4.0-10.0)	5.4 (3.6-7.8)	7.1 (4.5-12.7)	<0.001
- Lymphocyte level on admission* ⁺	0.8 (0.5-1.1)	1.0 (0.6-1.4)	0.8 (0.5-1.1)	<0.001
- Monocyte level on admission* ⁺	0.5 (0.3-0.7)	0.5 (0.3-0.7)	0.5 (0.3-0.7)	0.525
- Platelets on admission	210 (154-273)	214.0 (168-277)	199 (149-269)	0.265
- ESR level on admission	65 (36.8-95.3)	58 (30-90)	73.5 (40.0-97.8)	0.008
- PT on admission	11.1 (10.6-11.9)	10.9 (10.4-11.8)	11.4 (10.7-12.0)	0.028
- aPTT on admission	30.0 (27.0-34)	30.0 (27.0-33.8)	31.0 (27.0-34.0)	0.496
- D-dimer level on admission	0.6 (0.3-1.6)	0.4 (0.2-0.9)	0.7 (0.4-1.7)	<0.001
- CD4 ⁺ first recorded value* ⁺	242 (152.5-440.5)	270 (156-473)	225 (145-375)	0.117
- CD4 ⁺ T cells <200 cells/ml on admission ^{&}	83 (39.0%)	36 (35.3%)	47 (42.3%)	0.361
- CD8 ⁺ first recorded value* ⁺	141 (79.5-230.5)	173 (90-239.5)	121 (77-214)	0.035
- CD8 ⁺ T cells <100 cells/ml on admission ^{&}	137 (65.6%)	54 (54.5%)	83 (75.5%)	0.002
- First recorded CD4 ⁺ /CD8 ⁺ ratio* ⁺	1.9 (1.2-3.0)	1.8 (1.2-3.0)	2.1 (1.3-3.0)	0.308
- CD4 ⁺ on admission/CD4 ⁺ lower value	1.42 (1.00-3.07)	1.13 (1.00-2.80)	1.70 (1.03-3.87)	0.018
- CD8 ⁺ on admission/CD8 ⁺ lower value	1.55 (1.00-3.09)	1.31 (1.00-2.53)	1.72 (1.00-3.64)	0.035
- IL-6 first recorded value* ⁺	16.8 (5.1-49.4)	7.6 (3.2-24.6)	27.0 (9.8-77.5)	<0.001
- IL-6 first recorded >12 pg/ml ^{&}	123 (56.2%)	42 (39.3%)	81 (72.3%)	<0.001
- IL-10 first recorded value* ⁺	16.9 (98-35.4)	12.6 (8.9-24.1)	24.0 (12.0-44.6)	<0.001
- IL-10 first recorded >35 pg/ml ^{&}	48 (25.4%)	13 (14.3%)	35 (35.7%)	<0.001

Other infections				
- EBV infection/reactivation ^{&}	67 (48.2%)	21 (36.2%)	465 (56.8%)	0.026
- CMV infection/reactivation ^{&}	8 (6.1%)	2 (3.5%)	6 (7.4%)	0.356
- EBV and CMV infection or reactivation [#]	87 (62.6%)	27 (46.6%)	60 (74.1%)	<0.001
- Candida infection ^{&}	15 (7.4%)	3 (3.1%)	12 (11.3%)	0.051
- Staphylococcus infection ^{&}	41 (20.2%)	13 (13.5%)	28 (26.2%)	0.039
Pulmonary embolism (adverse effect or complication) ^{&}	28 (10.9%)	7 (5.4%)	21 (16.3%)	0.004
Hematology-DIC (adverse effect or complication) ^{&}	64 (24.8%)	24 (18.6%)	40 (31.0%)	0.031
Days hospitalized ^{*+}	10 (10-32)	11 (7-17)	29 (21.5-35)	<0.001
Length of hospitalization >12 days	104 (40.3%)	37 (28.7%)	67 (51.9%)	<0.001
Death ^{&}	144 (55.8%)	17 (13.2%)	127 (98.4%)	<0.001

Legend: CPR=cardiopulmonary resuscitation; APACHE=Acute Physiology and Chronic Health Evaluation; SOFA=Sequential Organ Failure Assessment; Na=sodium; K=potassium; Cl=chloride; HCO₃=bicarbonate; BUN=blood urea nitrogen; Cr=creatinine; CPK=creatinine phosphokinase; WBC=white blood cell; ESR=erythrocyte sedimentation rate; PT=prothrombin time; aPTT=activated partial thromboplastin time; IL-6=interleukin 6; IL-10=interleukin 10; EBV=Epstein-Barr virus; CMV=cytomegalovirus; DIC=disseminated intravascular coagulation.

*Median (p25-p75), ⁺Mann-Whitney U-test, [&]Chi-square test, [#]Fisher exact test.

Supplementary Table 3. Arrival method to the hospital (matched non-CPR group analysis)

	All	Matched non-CPR	CPR	p
n	258	129	129	
Arrived by their own means	177 (69.1%)	96 (75.6%)	81 (62.8%)	0.003
Transferred from another hospital	53 (20.6%)	15 (11.7%)	38 (29.5%)	
Ambulance	18 (7.0%)	10 (7.9%)	8 (6.2%)	
Long term facility or rehabilitation center	8 (3.1%)	6 (4.7%)	2 (1.6%)	

References

1. Al Amiry A, Maguire BJ. Emergency Medical Services (EMS) Calls During COVID-19: Early Lessons Learned for Systems Planning (A Narrative Review). *Open Access Emerg Med* 2021;13:407-14.
2. Serafim RB, Póvoa P, Souza-Dantas V, Kalil AC, Salluh JIF. Clinical course and outcomes of critically ill patients with COVID-19 infection: a systematic review. *Clin Microbiol Infect* 2021;27:47-54.
3. Ippolito M, Catalisano G, Marino C, Fucà R, Giarratano A, Baldi E, et al. Mortality after in-hospital cardiac arrest in patients with COVID-19: A systematic review and meta-analysis. *Resuscitation* 2021;164:122-9.
4. Bielski K, Makowska K, Makowski A, Kopiec T, Gasecka A, Malecka M, et al. Impact of COVID-19 on in-hospital cardiac arrest outcomes: An updated meta-analysis. *Cardiol J* 2021;28:816-24.
5. Mir T, Sattar Y, Ahmad J, Ullah W, Shanah L, Alraies MC, et al. Outcomes of in-hospital cardiac arrest in COVID-19 patients: A proportional prevalence meta-analysis. *Catheter Cardiovasc Interv* 2022;99:1-8.
6. Sultanian P, Lundgren P, Strömsöe A, Aune S, Bergström G, Hagberg E, et al. Cardiac arrest in COVID-19: characteristics and outcomes of in- and out-of-hospital cardiac arrest. A report from the Swedish Registry for Cardiopulmonary Resuscitation. *Eur Heart J* 2021;42:1094-106.
7. Beigmohammadi MT, Amoozadeh L, Rezaei Motlagh F, Rahimi M, Maghsoudloo M, Jafarnejad B, et al. Mortality Predictive Value of APACHE II and SOFA Scores in COVID-19 Patients in the Intensive Care Unit. *Can Respir J* 2022;2022:5129314.
8. Zou X, Li S, Fang M, Hu M, Bian Y, Ling J, et al. Acute Physiology and Chronic Health Evaluation II Score as a Predictor of Hospital Mortality in Patients of Coronavirus Disease 2019. *Crit Care Med* 2020;48:e657-65.
9. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
10. Zhu B, Feng X, Jiang C, Mi S, Yang L, Zhao Z, et al. Correlation between white blood cell count at admission and mortality in COVID-19 patients: a retrospective study. *BMC Infect Dis* 2021;21:574.
11. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, et al. Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia. *J Infect Dis* 2020;221:1762-9.
12. Jiang Y, Wei X, Guan J, Qin S, Wang Z, Lu H, et al. COVID-19 pneumonia: CD8⁺ T and NK cells are decreased in number but compensatory increased in cytotoxic potential. *Clin Immunol* 2020;218:108516.
13. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020;8:420-2.
14. Weiskopf D, Schmitz KS, Raadsen MP, Grifoni A, Okba NMA, Endeman H, et al. Phenotype and kinetics of SARS-CoV-2-specific T cells in COVID-19 patients with acute respiratory distress syndrome. *Sci Immunol* 2020;5:eabd2071.
15. Yi Y, Lagniton PNP, Ye S, Li E, Xu R-H. COVID-19: what has been learned and to be learned about the novel coronavirus disease. *Int J Biol Sci* 2020;16:1753-66.
16. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020;130:2620-9.