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Clinical paper

Clinical characteristics and outcomes of in-hospital cardiac arrest among patients with and without COVID-19

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Abstract

Aims: To define outcomes of patients with COVID-19 compared to patients without COVID-19 suffering in-hospital cardiac arrest (IHCA).

Materials and methods: We performed a single-center retrospective study of IHCA cases. Patients with COVID-19 were compared to consecutive patients without COVID-19 from the prior year. Return of spontaneous circulation (ROSC), 30-day survival, and cerebral performance category (CPC) at 30-days were assessed.

Results: Fifty-five patients with COVID-19 suffering IHCA were identified and compared to 55 consecutive IHCA patients in 2019. The COVID-19 cohort was more likely to require vasoactive agents (67.3% v 32.7%, p=0.001), invasive mechanical ventilation (76.4% v 23.6%, p<0.001), renal replacement therapy (18.2% v 3.6%, p=0.029) and intensive care unit care (83.6% v 50.9%, p=0.001) prior to IHCA. Patients with COVID-19 had shorter CPR duration (10 min v 22 min, p=0.002). ROSC (38.2% v 49.1%, p=0.336) and 30-day survival (20% v 32.7%, p=0.194) did not differ. A 30-day cerebral performance category of 1 or 2 was more common among non-COVID patients (27.3% v 9.1%, p=0.048).

Conclusions: Return of spontaneous circulation and 30-day survival were similar between IHCA patients with and without COVID-19. Compared to previously published data, we report greater ROSC and 30-day survival after IHCA in COVID-19.

Keywords: Cardiac arrest, COVID-19, Cardiopulmonary resuscitation, ROSC

Abbreviations: AHA, American Heart Association; CAD, Coronary artery disease; CKD, Chronic kidney disease; COVID-19, Coronavirus disease 2019; CPC, Cerebral performance category; DNR, Do not resuscitate; HLD, Hyperlipidemia; HTN, Hypertension; IHCA, In-hospital cardiac arrest; OHCA, Out-of-hospital cardiac arrest; PEA, Pulseless electrical activity; ROSC, Return of spontaneous circulation; VF, Ventricular fibrillation; VT, Ventricular tachycardia.

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Introduction

Coronavirus disease 2019 (COVID-19) is a global pandemic with more than 49 million cases and 1.2 million deaths worldwide, and >527,000 cases in New York State alone as of this writing. Among patients requiring hospitalization, mortality is reported in excess of 20% overall, and approximately 40% among patients with critical illness.[1,2] As the mortality among critically ill patients with COVID-19 is high, and risk of viral transmission to the clinical team is a significant consideration, the American Heart Association (AHA) suggests providers consider the appropriateness of initiating and continuing cardiopulmonary resuscitation (CPR) in this population.[3,4] To inform such decisions, a better understanding of clinical characteristics and outcomes of patients with COVID-19 suffering in-hospital cardiac arrest (IHCA) is required.

Prior to COVID-19, the rate of return of spontaneous circulation (ROSC) among patients with IHCA in the USA was up to 50% with survival to hospital discharge reported to be upward of 25%.[5] Among critically ill patients on invasive mechanical ventilation with IHCA, survival to discharge is lower than 15%.[4] There are limited data evaluating outcomes in patients with COVID-19 and IHCA.[5,6] The first published study of IHCA in COVID-19 demonstrated a rate of ROSC of 13.2%, with a 30-day survival of only 2.9%. However, asystole was the most common rhythm in this cohort and the authors raised concerns over shortage of medical resources and quality of CPR.[6] Similarly, a retrospective study of 31 patients with COVID-19 suffering IHCA at a New York City institution found that none survived to hospital discharge.[7]

Whether the initially-described poor outcomes were related to the disease process, degree of critical illness, or a function of provider and institutional approaches to COVID-19 patients with IHCA is unknown. We hypothesized that outcomes among COVID-19 patients with IHCA would be comparable to IHCA outcomes among non-COVID-19 patients with a similar degree of illness. To better address this question, we conducted a single-center retrospective study of IHCA among patients with COVID-19 compared to an equal number of consecutive IHCA patients from the year prior.

Methods

Setting and study design

This was a single-center retrospective observational study of IHCA at New York University (NYU) Langone Health: Manhattan Campus. The study was approved by the NYU Institutional Review Board (# s20-00831). At our institution, a dedicated IHCA team is called emergently to IHCA cases in the hospital via a paging system. Patients with "do not resuscitate" (DNR) orders do not undergo IHCA team activation. IHCA activation is otherwise universal among those on a general ward, but at the discretion of the intensivist among those in an intensive care unit (ICU). The critical care attending-led IHCA team consists of between two and four nurses specialized in the management of IHCA in accordance with the 2019 AHA guidelines. In addition to managing the IHCA, the team would document CPR start and stop times as well as additional intra-arrest events.

During the COVID-19 pandemic, a number of specific changes were made to our IHCA protocols. Providers responding to an IHCA were kept to the minimum number necessary. All responders were required to fully don personal protective equipment, including an N-95 mask, face shield, impermeable gown, and two sets of gloves prior to entering the room. Prior to IHCA team arrival, CPR was initiated by the first responder (usually the bedside nurse). However, the number of individuals allowed into a patient room was limited to 2 by contrast to the pre-COVID era where limits were not imposed. Use of a mechanical CPR device with the LUCAS 3.0™ chest compression system (Physio-Control, Redmond, WA) was standard-of-care during the pandemic. To decrease the risk of viral transmission, intubated patients were not disconnected from the ventilator for bag-valve ventilation. Extracorporeal cardiopulmonary resuscitation (ECPR) was not offered at our institution during this timeframe.

All patients >18 years of age diagnosed with COVID-19 (by positive PCR and documentation of COVID pneumonia in the chart) who suffered from IHCA and required IHCA team activation between March 25, 2020 and May 10, 2020 were recorded in our IHCA database and included in this study. At our institution, we maintain a database of IHCA activations as part of an ongoing quality improvement initiative. Cases of IHCA not undergoing IHCA team activation were not tracked in the database and were therefore excluded from the study. An equal number of consecutive patients without COVID-19 with IHCA from March 25, 2019 to October 04, 2019 were selected for comparison.

Data collection and definitions

Patient characteristics, demographics, and clinical comorbidities, were abstracted from the medical record. The IHCA database provided patient names and identifiers as well as the start and stop time of the IHCA. All additional data required chart review. Baseline co-morbid conditions (such as hypertension, metastatic cancer, coronary artery disease) were defined as being present when documented by the admitting provider in the history and physical exam note on index admission. Chronic kidney disease (CKD) was defined as stage III or greater. Pre-IHCA conditions were defined as existing within the 24 h prior to IHCA. These conditions included hypotension, vasopressor or inotrope requirement, invasive mechanical ventilation, hypotension, and requirement for renal replacement therapies. Hypotension was defined as a documented mean arterial pressure of <65 mmHg over a 30-minute period or the need for vasopressor infusion.

Clinical documentation of the IHCA, including initial electrocardiographic rhythm, CPR start and stop times, medication administration, and defibrillation were reviewed. CPR duration was determined by timestamped start and stop times documented by the team in the medical record. Pulseless electrical activity (PEA), asystole, and ventricular tachycardia (VT) or ventricular fibrillation (VF) were deemed initial IHCA rhythms when documented as such in the medical record. Causes of cardiac arrest were determined by medical record review and attending documentation in the event note or discharge summary. Cardiac etiology of arrest was defined by cardiogenic shock or malignant arrhythmia as most likely cause of arrest as deemed by the attending provider. A respiratory etiology of arrest was documented when the cause was felt to be related to significant or worsening hypoxemia, hypercapnia, endotracheal tube obstruction, or pneumothorax.

Pulmonary embolism (PE) was considered likely based on IHCA attending assessment. Our primary outcome was ROSC (defined as sustained ROSC, or palpable pulse without ongoing CPR, for > 20 min). Secondary outcomes were 30-day survival, and cerebral performance category (CPC) of 1 or 2 at 30-days. A CPC of 1 was defined by good cerebral performance (normal life with at most minor neurologic deficits) and a CPC of 2 was defined by moderate cerebral disability. [4] The CPC was determined via neurological assessment obtained via chart review at the 30-day mark.

Statistical analysis

Patient demographics and clinical characteristics were presented using percentages for categorical variables and median, interquartile range (IQR) for continuous variables. The Chi-squared test was used to analyze associations between categorical variables while the Fisher's exact test was used for cases in which there were fewer than 5 observations per group. Mann-Whitney U tests were used to analyze differences in means for continuous variables. A two-tailed p-value <0.05 was used to establish the statistical significance. Statistical analyses were carried out in R (Version 3.5.1).

Results

Between March 25, 2020 and May 10, 2020 there were 3675 COVID-positive patients admitted to the hospital, 810 deaths, and 55 IHCA cases requiring IHCA team activation. Only 4 cases of IHCA were COVID negative during this timeframe and were not included in the analysis. The total number of IHCA cases not requiring IHCA team activation was unknown. In the year prior to the COVID-19 pandemic, from March 01, 2019 and October 04, 2019, there were a total of 40,029 admissions, 608 deaths, and 55 IHCA team activations that served as the reference group. This pre-COVID period was selected to provide an equal number of cases as during the COVID timeframe. The incidence of IHCA was 1.5% during the COVID surge and 0.13% pre-COVID.

Table 1 displays demographics and pre-arrest characteristics of COVID-19 and non-COVID-19 patients. The average age among COVID-19 patient suffering IHCA was 67 years old ($\pm$15) and 87.3% were men. In contrast, 60% of non-COVID-19 patients were men ($p=0.002$). Non-COVID-19 patients were more likely to have stage $\geq$3 chronic kidney disease (CKD) (30.9% vs. 9.1%, $p=0.009$) and coronary artery disease (CAD) (60% vs. 14.5%, $p<0.001$) compared to COVID-19 patients. Compared to non-COVID-19 patients, those with COVID-19 were more likely to require vasoactive agents (67.3% v 32.7%, $p=0.001$), invasive mechanical ventilation (76.4% vs. 23.6%, $p<0.001$), renal replacement therapy (18.2% v 3.6%, $p=0.029$) and intensive care unit (ICU) care (83.6% vs. 50.9%, $p=0.001$) prior to the IHCA.

Table 2 provides characteristics of patients with and without COVID-19 during, and post cardiac arrest. COVID-19 patients were less likely to have a cardiac cause of arrest (9.1% v 34.5%) and were more likely to have a respiratory cause of arrest (49.1% v 21.8%). The most frequent rhythm encountered among those with COVID-19 was pulseless electrical activity (PEA) (74.5%) and did not differ significantly from the non-COVID-19 patients. During IHCA, the average duration of CPR was shorter among patients with versus without COVID-19 (median 10 min vs. 22 min, $p=0.002$). The rate of ROSC (38.2% v 49.1%, $p=0.336$) and 30-day survival (20% v 32.7%, $p=0.194$) did not differ between the groups. A greater proportion of non-COVID-19 patients had a 30-day CPC of $\leq$2 than COVID-19 patients (27.3% v 9.1%, $p=0.048$). None of the reported continuous variables were normally distributed.

Table 1 – Demographics and Pre-arrest Characteristics of Patients with and without COVID-19.

Variable	COVID (n=55)	Non-COVID (n=55)	p-value
Demographics & Comorbidities			
Age (median [IQR])	69.00 [64.00, 77.00]	69.00 [58.50, 79.00]	0.867
Male Sex (n, %)	48 (87.3)	33 (60.0)	0.002
Race/Ethnicity			
White non-Hispanic (n, %)	35 (63.6)	35 (63.6)	0.892
Black non-Hispanic (n, %)	7 (12.7)	7 (12.7)	
Hispanic (n, %)	8 (14.5)	6 (10.9)	
Other (n, %)	5 (9.1)	7 (12.7)	
Hypertension (n, %)	39 (70.9)	37 (67.3)	0.837
Dyslipidemia (n, %)	18 (32.7)	24 (43.6)	0.326
Diabetes Mellitus (n, %)	17 (30.9)	23 (41.8)	0.322
Coronary Artery Disease (n, %)	8 (14.5)	33 (60.0)	<0.001
Chronic Kidney Disease (n, %)	5 (9.1)	17 (30.9)	0.009
Cirrhosis (n, %)	0 (0.0)	5 (9.1)	0.057
Pre-IHCA Conditions			
Hypotension (n, %)	42 (76.4)	24 (43.6)	0.001
Metastatic Cancer (n, %)	1 (1.8)	9 (16.4)	0.016
Hepatic Insufficiency (n, %)	0 (0.0)	3 (5.5)	0.243
Renal Insufficiency (n, %)	23 (41.8)	19 (34.5)	0.556
Medical Service (n, %)	55 (100.0)	45 (81.8)	0.001
Surgical Service (n, %)	0 (0.0)	10 (18.2)	
On Pressor or Inotrope (n, %)	37 (67.3)	18 (32.7)	0.001
Invasive Ventilation (n, %)	42 (76.4)	13 (23.6)	<0.001
Renal Replacement Therapy (n, %)	10 (18.2)	2 (3.6)	0.029

Variables are expressed as n (%), and median [interquartile range].
COVID: coronavirus disease, IHCA: in-hospital cardiac arrest.

Table 2 – Characteristics of patients with and without COVID-19 during and post cardiac arrest.

Variable	COVID (n=55)	Non-COVID (n=55)	p-value
Event Location			
ICU (n, %)	46 (83.6)	28 (50.9)	0.001
Ward (n, %)	9 (16.4)	22 (40.0)	
ED (n, %)	0 (0.0)	2 (3.6)	
Procedure Area (n, %)	0 (0.0)	3 (5.5)	
IHCA Characteristics			
CPR Duration (min) (median [IQR])	10.00 [5.00, 18.00]	22.00 [8.00, 50.50]	0.002
Initial rhythm			
VF/VF (n, %)	6 (10.9)	9 (16.4)	0.429
PEA (n, %)	41 (74.5)	42 (76.4)	
Asystole (n, %)	8 (14.5)	4 (7.3)	
ECPR (n, %)	0 (0.0)	5 (9.1)	0.057
Post-IHCA			
Targeted Temperature Management (n, %)	3 (5.5)	14 (25.5)	0.007
Emergent Angiography (n, %)	1 (1.8)	5 (9.1)	0.206
ROSC (n, %)	21 (38.2)	27 (49.1)	0.336
30 Day Survival (n, %)	11 (20.0)	18 (32.7)	0.194
CPC 1–2 at 30 Days (n, %)	5 (9.1)	15 (27.3)	0.048
Cause of Arrest			
Cardiac (n, %)	5 (9.1)	19 (34.5)	0.001
Respiratory (n, %)	27 (49.1)	12 (21.8)	
Pulmonary Embolism (n, %)	7 (12.7)	4 (7.3)	
Other (n, %)	16 (29.1)	20 (36.4)	

Variables are expressed as n (%), and median [interquartile range]. ICU: intensive care unit, ED: emergency department, CPR: cardiopulmonary resuscitation, IHCA: In-hospital cardiac arrest, VT: ventricular tachycardia, VF: ventricular fibrillation, PEA: pulseless electrical activity, ECPR: extracorporeal cardiopulmonary resuscitation, ROSC: return of spontaneous circulation, CPC: cerebral performance category.

Discussion

Compared to non-COVID-19 patients at our institution, patients with COVID-19 were more likely to have a respiratory cause of arrest with a similar rate of PEA. While the median duration of CPR was significantly shorter in the COVID-19 cohort (10 min v 22 min, p=0.002), rate of ROSC and 30-day survival were similar (38.2 v 49.1%, p=0.336 for ROSC and 20% v 32.6%, p=0.194 for 30-day survival). This is in stark contrast to a recent 136-patient cohort from Wuhan that reported substantially lower rates of ROSC (13.2% vs. 38.2%) and 30-day survival (2.9% vs. 20%). Only one patient in the study survived with good neurological function.[6] Such discordant outcomes may reflect important differences in IHCA in these two groups, including a substantially lower rate of asystole as initial rhythm at our center (14.5% vs. 89.7%).[6,8] More extensive information on the degree of critical illness was not provided in the Wuhan cohort nor was the median duration of CPR. Similarly, poor outcomes were demonstrated in a cohort of 31 patients with COVID-19 suffering cardiac arrest at a New York City institution; 42% of patients achieved ROSC while no patient survived to hospital discharge.[7]

Using the Get-With-The-Guidelines registry, Girotra et al. identified 5690 patients with pneumonia or sepsis on mechanical ventilation with IHCA, a cohort that was chosen to be comparable to patients with IHCA from COVID-19. Among patients in the 60–69 age range suffering PEA or asystole, the survival to discharge was 11.1% and 5.6% for those on vasopressors.[4] The survival to discharge with a CPC of 1–2 was 8.2% in this group and 4.0% among those on vasopressors. While we report a somewhat higher survival rate than this historical cohort, we evaluated 30-day outcomes and survival to discharge may, in fact, be lower. However, the outcomes presented by Girotra et al. are superior to those of the Wuhan cohort. In a large multicenter cohort of critically ill patients with COVID-19 suffering IHCA, 12% survived to hospital discharge while 7% survived with either normal or mildly impaired neurologic status.[9] While we demonstrated somewhat higher rates of survival, we explored 30-day outcomes and used a mixed population including patients with IHCA outside the critical care setting.

In our cohort, those with COVID-19 IHCA in our cohort had a high burden of critical illness with a higher likelihood or requiring vasopressors, invasive mechanical ventilation, renal replacement therapies, and ICU admission than the non-COVID-19 cohort. Causes of IHCA also differed between the two groups: patients with COVID-19 were more likely to have a respiratory cause of arrest and less likely to arrest from cardiac causes. Presenting rhythms were similar between the two cohorts. While ROSC and 30-day survival were similar, those with COVID-19 had worse neurological outcomes at the 30-day mark.

The median duration of CPR was significantly shorter among patients with COVID-19 compared to non-COVID-19 patients with similar rates of ROSC between the 2 cohorts at our center. While the number of patients achieving ROSC and surviving for 30-days are low, these findings may suggest a more rapidly reversible cause of cardiac arrest. Approximately 50% of COVID-19 patients suffering IHCA had a respiratory etiology of their arrest; brief episodes of hypoxia while on mechanical ventilation may have been quick to improve or normalize during the IHCA when compared to other causes of arrest more often encountered in non-COVID-19 patients. Interestingly, despite similar rates and ROSC and 30-day survival, a greater number of patients with COVID had critical illness based on the need for vasoactive agents, invasive mechanical ventilation, and renal replacement therapies prior to the arrest. In contrast, non-COVID-19 patients had a higher burden of comorbid disease such as coronary artery disease, chronic kidney disease, and metastatic cancer which may have factored into the outcomes.

Fewer COVID-19 patients achieved a CPC of 1 or 2 at 30-days compared to non-COVID patients. COVID-19 has been associated with a range of neurological manifestations, which may, in part, explain this difference.[10] Plausibly, after a longer period of observation, more COVID-19 patients may achieve a more favorable CPC. Although mortality was not significantly different at 30-days between the cohorts, we did not assess long-term survival.

Important differences exist between those with, and without COVID-19 suffering cardiac arrest speaking to the impact of the pandemic. Decreased survival has been demonstrated among COVID-19 patients with IHCA as well as out-of-hospital cardiac arrest (OHCA).[7,11,12] Cardiac arrest among COVID-19 patients is more likely to be related to a non-shockable rhythm; a known factor associated with worse prognosis.[6,11] In OHCA, the rate of bystander CPR has been demonstrated to be significantly lower with delayed emergency medical arrival by contrast to the pre-pandemic period potentially explaining worse outcomes.[11] Concerning the in-hospital setting, delays in CPR initiation may have also occurred and in part be attributed to time necessary to don personal protective equipment and overstretched providers.

There are a number of important limitations of this study. First, the sample size was small. Although consecutive cases from 2019 were used as a reference group, matching based on demographic or clinical covariates was not performed. We do not have information on those who died without resuscitation attempts to compare to those who underwent CPR. While all patients were placed on cardiac monitoring on admission, we were unable to ascertain if monitoring was removed for any reason prior to arrest. Due to the retrospective nature of our study, we did not have information regarding time to CPR initiation nor time to defibrillation among cases of VT or VF. Further, we relied on IHCA team documentation of cardiac arrest start and stop times and primary team documentation of events surrounding the arrest; the accuracy of the documentation can be reasonably called into question.

Only patients with cardiac arrest requiring IHCA team activation were included in this analysis; the cohort receiving CPR by the treating team without IHCA team activation was excluded and data on this group is not available. Based on the mortality at our institution in this timeframe, our report is likely an incomplete sample of all IHCA during this time period. Similarly, IHCA team activation did not occur in patients with a DNR order. Difference in the use of palliative care consultation and variation in DNR code status between calendar years cannot be excluded and may represent a source of bias.

Conclusions

In a single-center study of patients suffering IHCA, we demonstrated a comparable rate of ROSC and 30-day survival among those with and without COVID-19 with a lower rate of favorable neurological outcomes at 30-days among COVID-19 patients. Outcomes of IHCA in COVID-19 reported in the present study are superior to some of those previously published. These data may be useful to providers to determine the thresholds to initiate and terminate resuscitative efforts. Further studies with larger numbers of patients are necessary to identify predictors of favorable outcomes after IHCA in COVID-19.

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Declaration of conflicts of interest

EY, OJLM, SBB, AG, YX, and SP have no conflicts of interest to declare. JMH receives funding from Inari Medical.

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