Survival After In-Hospital Cardiac Arrest In Critically Ill Patients: Implications For COVID-19 Outbreak?

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Keywords

COVID-19; in-hospital cardiac arrest; survival outcomes

The coronavirus disease 2019 (COVID-19) outbreak is placing a considerable strain on U.S. healthcare systems by requiring both significant acute resources and endangering healthcare team members through airborne infection.[1] Many U.S. healthcare systems are now considering how to treat COVID-19 patients who suffer cardiac arrest based on a presumption of poor survival after resuscitation in COVID-19 patients.[2] However, empiric data on cardiac arrest survival in COVID-19 from the United States are not available at the moment. To inform this debate, we report survival data following cardiopulmonary resuscitation in a cohort of critically ill patients with pneumonia or sepsis who were receiving mechanical ventilation in an intensive care unit (ICU) at the time of arrest.

Using Get-With-The-Guidelines-Resuscitation, a U.S. registry of in-hospital cardiac arrest patients, [3] we identified all adult patients (age 18 years and older) who underwent cardiopulmonary resuscitation for an index in-hospital cardiac arrest event. To simulate our study cohort as closely as possible to the COVID-19 population, we restricted our cohort to 5690 patients hospitalized in an ICU with a diagnosis of pneumonia or sepsis during the hospitalization and who were receiving mechanical ventilation at the time of arrest during 2014-2018. The study outcomes included survival to discharge, survival with a cerebral performance category (CPC) score of 1 (none to mild neurological disability), and survival with a CPC of 1 or 2 (no worse than moderate disability). We examined the above survival outcomes overall, and stratified by patient age (categorized as <50, 50-59, 60-69, 70-79, and

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80 years), initial rhythm (asystole or pulseless electrical activity [PEA] vs. ventricular fibrillation [VF] or pulseless ventricular tachycardia [VT]) and whether patients were receiving intravenous vasopressors at the time of arrest. All analyses were carried out using SAS. The study was reviewed by Saint Luke's Hospital's Mid America Heart Institute Institutional Review Board which waived the requirement for informed consent. Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to Get With The Guidelines-Resuscitation (GWTGResuscitationResearch@heart.org).

The median age was 65 years. All patients were located in an ICU and were receiving mechanical ventilation at the time of arrest. The initial cardiac arrest rhythm was asystole or PEA in a majority (87%) of patients and more than half (57%) were also receiving intravenous vasopressors at the time of arrest. The overall rate of survival to discharge was 12.5%. Rate of survival with CPC of 1 or 2 was 9.2% and survival with CPC of 1 was 6.2%.

Table includes rates of overall survival, survival with a CPC of 1 or 2, and survival with a CPC of 1 across categories of age-group, initial rhythm and need for vasopressors. Older age, initial rhythm of asystole or PEA and use of vasopressors were associated with worse survival outcomes. In patients 80 years old with asystole or PEA on mechanical ventilation, the overall rate of survival was 6%, and survival with CPC of 1 or 2 was 3.7%. Survival with CPC of 1 in that group was 1.7%. Among all patients with asystole or PEA who were also receiving vasopressors (n=2845, 50% of the cohort), less than 10% of patients were discharged with a CPC of 1 or 2 and less than 7% were discharged with a CPC of 1, across all age groups. The corresponding rates of survival with a CPC of 1 or 2, and CPC of 1 were 2.7% and 1.2% in the 80 years age group with asystole/ PEA and on vasopressors. Similar patterns of survival by age and vasopressor use were noted in patients with VF or pulseless VT, although the overall rates were higher compared to patients with asystole or PEA. In patients <50 years of age, with VF or pulseless VT who were not on vasopressors, overall survival was 26.1%, survival with a CPC of 1 or 2 was 22.0%, and survival with CPC of 1 was 16.5%.

We believe that these data can help inform discussions among patients, providers and hospital leaders regarding resuscitation policies and goals of care in the context of the COVID-19 pandemic which is posing unprecedented challenges to the U.S. healthcare system. The limited supply of ICU beds, mechanical ventilators and personal protective equipment (PPE) is already placing a tremendous strain on health systems. That notwithstanding, a recent article in the *Washington Post* noted that some hospitals are already considering universal do-not-resuscitation orders in patients with confirmed COVID-19 potentially overriding wishes of patients and their families for resuscitation.[2] Furthermore, a recent discussion in the *BMJ* highlighted similar challenges in how to perform resuscitation effectively under these circumstances.[4]

Although empirical data regarding resuscitation outcomes in COVID-19 patients from the U.S. are not available at the moment, a recent study from Wuhan, China found an overall survival of 2.9% in 136 COVID-19 patients who underwent cardiopulmonary resuscitation for in-hospital cardiac arrest.[5] However, extrapolation of these findings to the U.S. needs to

be done with caution. First, in-hospital cardiac arrest survival in China prior to the COVID-19 pandemic are important for context. A 2016 study from Beijing that included 1292 patients with in-hospital cardiac arrest from 12 hospitals found an overall survival of 9.1%, [6] which is much lower compared to a median survival of ~25% in the U.S. Second, it is possible that the poor survival in COVID-19 patients reported in the study from Wuhan are in part, because the hospital was severely overwhelmed with COVID-19 patients and struggled to provide ICU care and ventilatory support for many severely ill patients (83% of patients included in the study had a cardiac arrest on the wards).

Until empirical data on cardiac arrest survival for COVID-19 patients in the U.S. become available, we believe that our study findings can help inform the debate about resuscitation care for COVID-19 patients in the U.S. While we found low overall rates of survival and neurological outcomes in a cohort of selected ICU patients that would be most similar to critically ill COVID-19 patients, large heterogeneity in survival outcomes based on patient, cardiac arrest and treatment variables was still present. The probability of survival without severe neurological disability (CPC of 1 or 2) ranged from less than 3% to over 22% across key patient subgroups, while survival with none to mild disability (CPC of 1) ranged from ~1% to 16.5% Such large variation in survival rates suggest that a blanket prescription of do-not-resuscitate orders in patients with COVID-19 may be unwarranted. Such a blanket policy also ignores the fact that early experience of the pandemic in the U.S. reveals that a large proportion of COVID-19 patients are <50 years of age and otherwise healthy.[7] Cardiac arrest in such patients will likely have a different prognosis. Moreover, while asystole or PEA may be more common rhythms in the event of a cardiac arrest in COVID-19 patients due to the associated hypoxia and respiratory failure, patients may also develop ventricular arrhythmias due to associated myocarditis, and QTc prolongation (e.g., due to treatments like hydroxychloroquine) which may be reversible. We believe that absent survival data for resuscitation in COVID-19 patients, clinicians could use data on survival presented here to engage patients and families in meaningful conversations regarding the likelihood of survival in the event of a cardiac arrest based on age, presenting rhythm and illness severity.

Our findings should be interpreted carefully. Although we selected our cohort to be as closely representative of COVID-19 patients as possible (i.e., patients with pneumonia or sepsis on ventilatory support in an ICU at the time of arrest), the survival rates reported here represent a 'best-case scenario'. It is possible that COVID-19 patients who arrest are sicker and may therefore experience lower survival. Moreover, resuscitation care in COVID-19 patients in healthcare settings is likely to be delayed due to the need for donning PPE which may lead to worse survival in COVID-19 patients. Second, the definition of pneumonia and sepsis used in this study is based on documentation in the medical record which may differ from other criteria (e.g., diagnosis codes) used for identifying similar patients. Third, data on CPC scores were missing in 25.8% of all survivors which was similar across patient subgroups. Therefore, calculations of neurological outcomes were based on the proportion of survivors with CPC 1 or CPC 1 and 2 among those with documented CPC scores. Finally, it is likely that hospitals participating in Get With The Guidelines-Resuscitation are motivated for improving resuscitation care quality and their experience may not be representative of non-participating hospitals.

In conclusion, we found that in a cohort of critically ill patients on mechanical ventilation, survival outcomes following in-hospital resuscitation were not uniformly poor. These data may help guide discussions between patients, providers and hospital leaders in discussing appropriate use of resuscitation for COVID-19 patients.

Acknowledgments

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Table.

Rates of Survival to Discharge, Survival with a CPC of 1 or 2, and Survival with a CPC of 1 by Age-Group, Cardiac Arrest Rhythm, and Vasopressor Status.

	ASYSTOLE / PEA		VF / PULSELESS VT	
AGE GROUP	**All patients**	**Patients on vasopressors**	**All patients**	**Patients on vasopressors**
<50 years				
N	980	562	111	67
Survival to discharge	16.8%	10.1%	26.1%	17.9%
Survival with a CPC of 1 or 2 [*]	12.9%	8.3%	22.0%	15.9%
Survival with a CPC of 1 [†]	9.9%	6.3%	16.5%	11.9%
50-59 years				
N	945	533	163	103
Survival to discharge	12.1%	5.1%	26.4%	23.3%
Survival with a CPC of 1 or 2 [*]	8.9%	3.4%	19.6%	18.6%
Survival with a CPC of 1 [†]	6.3%	2.7%	14.5%	15.5%
60-69 years				
N	1305	773	198	107
Survival to discharge	11.1%	5.6%	20.7%	15.0%
Survival with a CPC of 1 or 2 [*]	8.2%	4.0%	14.3%	12.3%
Survival with a CPC of 1 [†]	4.8%	2.4%	9.3%	6.8%
70-79 years				
N	1110	645	169	103
Survival to discharge	8.6%	4.8%	20.1%	13.6%
Survival with a CPC of 1 or 2 [*]	6.0%	3.0%	14.7%	12.5%
Survival with a CPC of 1 [†]	3.6%	2.1%	10.1%	7.9%
80 years				
N	629	332	80	47
Survival to discharge	6.0%	3.9%	15.0%	10.6%
Survival with a CPC of 1 or 2 [*]	3.7%	2.7%	6.8%	6.4%
Survival with a CPC of 1 [†]	1.7%	1.2%	5.5%	6.4%

Abbreviations: PEA: pulseless electrical activity; VF: ventricular fibrillation; VT: ventricular tachycardia

[*] To address missing data on CPC scores, rates of survival with CPC of 1 or 2 were calculated by determining the proportion of survivors with CPC of 1 or 2 among all survivors with available CPC data and multiplying that proportion by the overall survival rate.

[†] Similarly, rates of survival with CPC of 1 were calculated by determining the proportion of survivors with CPC of 1 among all survivors with available CPC data and multiplying that proportion by the overall survival rate.