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Short paper

Outcomes of pediatric patients with COVID-19 and in-hospital cardiopulmonary resuscitation

Rayan S. El-Zein\textsuperscript{a,b,*}, Maya L. Chan\textsuperscript{c}, Lillian Su\textsuperscript{d}, Paul S. Chan\textsuperscript{a,b}, for the American Heart Association’s Get With the Guidelines\textsuperscript{®}-Resuscitation Investigators

\textsuperscript{a} Saint Luke’s Mid America Heart Institute, Kansas City, MO, United States
\textsuperscript{b} University of Missouri-Kansas City, Kansas City, MO, United States
\textsuperscript{c} William College, Williamstown, MA, United States
\textsuperscript{d} Stanford University School of Medicine, Palo Alto, CA, United States

Abstract

Background: Early studies found low survival rates for adults with COVID-19 infection and in-hospital cardiac arrest (IHCA). We evaluated the association of COVID-19 infection on survival outcomes in pediatric patients undergoing cardiopulmonary resuscitation (CPR).

Methods: Within Get-With-The-Guidelines\textsuperscript{®}-Resuscitation, we identified pediatric patients who underwent CPR for an IHCA or bradycardia with poor perfusion between March and December, 2020. We compared survival outcomes (survival to discharge and return of spontaneous circulation for \textgreek{≥}20 minutes [ROSC]) between patients with suspected/confirmed COVID-19 infection and non-COVID-19 patients using multivariable hierarchical regression, with hospital site as a random effect and patient and cardiac arrest variables with a significant ($p < 0.05$) bivariate association as fixed effects.

Results: Overall, 1328 pediatric in-hospital CPR events were identified (590 IHCA, 738 bradycardia with poor perfusion), of which 46 (32 IHCA, 14 bradycardia) had suspected/confirmed COVID-19 infection. Rates of survival to discharge were similar between those with and without COVID-19 infection (39.1% vs. 44.9%; adjusted RR, 1.14 [95% CI: 0.55–2.36]), and these estimates were similar for those with IHCA and bradycardia with poor perfusion (adjusted RRs of 1.03 and 1.05; interaction $p = 0.96$). Rates of ROSC were also similar between pediatric patients with and without COVID-19 overall (67.4% vs. 76.9%; adjusted RR, 0.87 [0.43, 1.77]), and for the subgroups with IHCA or bradycardia requiring CPR (adjusted RRs of 0.95 and 0.86, interaction $p = 0.26$).

Conclusions: In a large multicenter national registry of CPR events, COVID-19 infection was not associated with lower rates of ROSC or survival to hospital discharge in pediatric patients undergoing CPR.

Keywords: In-hospital cardiac arrest, COVID-19, Cardiopulmonary resuscitation, Pediatric cardiac arrest

Introduction

Although coronavirus disease 2019 (COVID-19) has been described primarily as a mild disease in children, rates of pediatric hospitalizations of patients with COVID-19 are on the rise.\textsuperscript{7} The hospital course of pediatric patients may be complicated by clinical decompensation and potentially progress to in-hospital cardiac arrest (IHCA), yet little information is currently available on outcomes of pediatric patients with COVID-19 undergoing cardiopulmonary resuscitation (CPR).

Abbreviations: IHCA, in-hospital cardiac arrest, COVID-19, coronavirus disease 2019, CPR, cardiopulmonary resuscitation, GWTG-R, Get With The Guidelines Resuscitation Registry

* Corresponding author at: Saint Luke’s Mid America Heart Institute, 4401 Wornall Rd, Kansas City, MO 64111, United States.
E-mail address: Rel-zein@saint-lukes.org (R.S. El-Zein).

https://doi.org/10.1016/j.resuscitation.2022.02.018

Received 24 November 2021; Received in Revised form 15 February 2022; Accepted 20 February 2022

0300-9572/© 2022 Published by Elsevier B.V.
In adults with COVID-19 infection, previous reports have described low survival rates for those with IHCA.\(^2\)\(^-\)\(^4\) Besides the physiologic effects of COVID-19 infection, other potential reasons for lower survival in adults with IHCA include delays in CPR initiation due to requirements of donning personal protective equipment, shorter duration of resuscitation efforts, and overall decrease in CPR quality.\(^5\)\(^,\)\(^6\) Although it would be reasonable to believe that pediatric patients with COVID-19 who undergo CPR would have lower survival than children without COVID-19, there is a need for empirical data to quantify the extent of lower survival with COVID-19 infection in this population. Accordingly, within a large national registry, we examined the association of COVID-19 infection on survival outcomes for pediatric patients who underwent CPR.

**Methods**

The study was approved by Saint Luke’s Hospital’s IRB, which waived the requirement for informed consent as the study involved deidentified data.

**Study design**

Get With The Guidelines\(^7\) (GWTG)-Resuscitation is a large, prospective, quality improvement registry of IHCA and CPR events. The registry design has been previously described.\(^7\) In brief, trained hospital personnel identify all patients without do-not-resuscitate orders who undergo cardiopulmonary resuscitation. Cases are identified by centralized collection of cardiac arrest flow sheets, reviews of hospital paging system logs, and routine checks of code carts and pharmacy tracer drug records.\(^7\) Standardized Utstein-style definitions are used for all patient variables and outcomes to facilitate uniform reporting across hospitals.\(^8\)\(^,\)\(^9\)

Within GWTG-Resuscitation, we identified patients under 18 years of age between March 1 and December 31, 2020, with an in-hospital CPR event due to a pulseless IHCA or bradycardia with poor perfusion requiring CPR. The independent variable was whether the pediatric patient had suspected/confirmed COVID-19 infection at the time of their CPR event. Our primary outcome was survival to discharge, and the secondary outcome was sustained return of spontaneous circulation for \(\geq 20\) minutes (ROSC).

**Statistical analysis**

Baseline characteristics of patients with and without COVID-19 were compared using Fisher’s exact test for categorical variables and student’s \(t\)-test for continuous variables.

In the overall cohort, we compared rates of survival to discharge between patients with and without COVID-19 infection by constructing multivariable hierarchical regression models, with hospital site as a random effect and COVID-19 status, location of arrest, and initial rhythm, regardless of statistical significance as fixed effects. Because of the sample size, we only included the following other variables with a bivariate association as fixed effects to avoid over-parameterization: age, sex, race, initial cardiac arrest rhythm, location of cardiac arrest, comorbid conditions (prior heart failure or myocardial infarction, index admission heart failure or myocardial infarction, diabetes mellitus, baseline depression in central nervous system function, acute stroke, pneumonia, and metastatic or hematologic malignancy), medical conditions present within 24 hours of cardiac arrest (renal insufficiency, hepatic insufficiency, respiratory insufficiency, hypotension, septicemia, and metabolic or electrolyte abnormality), and interventions in place at the time of cardiac arrest (continuous intravenous vasopressor, assisted or mechanical ventilation, and hemodialysis). These models used a Poisson distribution with a log-link to estimate risk ratios (RRs). We then evaluated for an interaction between COVID-19 status and CPR event type (IHCA vs. bradycardia with poor perfusion) to determine if the association between COVID-19 and survival differed for IHCA and bradycardia events. Finally, we repeated all analyses for the secondary outcome of ROSC.

For each analysis, the null hypothesis was evaluated at a 2-sided significance level of 0.05 and calculated 95% confidence intervals (CIs) using robust standard errors. All statistical analyses were conducted using SAS Version 9.1.3 (SAS Institute, Cary, NC).

**Results**

Of 1328 pediatric in-hospital CPR events, 590 were pulseless IHCAs and 738 were bradycardia requiring CPR. Suspected/confirmed COVID-19 infection was present in 46 patients (17 confirmed, 6 suspected, and 23 were missing designation as confirmed or suspected). Of these 46 with suspected/confirmed COVID-19 infection, 32 (5.4%) had IHCA and 14 (1.9%) had bradycardia requiring CPR. Patient and cardiac arrest characteristics by COVID-19 status and CPR event type (pulseless IHCA and bradycardia with poor perfusion) are summarized in Table 1. Both cohorts were similar in age groups, sex, race/ethnicity, and an initial non-shockable cardiac arrest rhythm. Compared with non-COVID-19 patients, COVID-19 patients were more likely to have sepsis, pneumonia, and renal insufficiency. Rates of continuous intravenous vasopressor agents, invasive mechanical ventilation, and hemodialysis at the time of arrest were comparable in both groups.

Overall, 18 (39.1%) COVID-19 patients with a CPR event survived to discharge as compared with 576 (44.9%) non-COVID-19 patients. After multivariable adjustment, COVID-19 infection was not associated with survival to discharge overall (adjusted RR, 1.14 [95% CI: 0.55, 2.36]), and this was the case separately for IHCA and bradycardia requiring CPR (adjusted RRs of 1.03 and 1.05, respectively; interaction \(p\)-value: 0.96; Table 2). COVID-19 infection was also not associated with reduced rates of ROSC as compared to non-COVID-19 patients (67.4% vs. 76.9%; adjusted RR, 0.87 [0.43, 1.77]), with no difference in ROSC rates for patients with either IHCA or bradycardia requiring CPR (adjusted RRs of 0.95 and 0.86, respectively; interaction \(p\)-value: 0.26).

**Discussion**

Among pediatric patients requiring CPR during the pandemic months in 2020, COVID-19 infection was not associated with lower rates of ROSC or survival to discharge. This was the case overall, and for those with IHCA or bradycardia with poor perfusion. Our results on the association between COVID-19 infection and survival differ from those for IHCA in adult patients, which ranged from 0% to 14%.\(^10\)\(^,\)\(^11\)

One reason for the difference in results is potentially less severe illness with COVID-19 in hospitalized pediatric patients undergoing CPR as compared to adults. In our study, there were no differences in rates of mechanical ventilation between pediatric patients requiring CPR with and without COVID-19 infection although there were higher rates of pneumonia and sepsis in pediatric patients with
COVID-19. Less severe respiratory compromise in pediatric COVID-19 patients with a CPR event may account for the different associations of COVID-19 infection in pediatric and adult patients with CPR events. Although some have questioned whether CPR should even be initiated in adults with COVID-19 infection and IHCA,12,13 our findings suggest that end-of-life decisions for pedi-

| Table 1 – Baseline characteristics of patients with and without COVID-19 infection.* |
|---------------------------------|---------------------------------|---------------------------------|
|                                 | Pulseless IHCA (N = 590)        | Bradycardia (N = 738)            |
| Total                           | No COVID-19 (n = 558)           | COVID-19 + (n = 32)              |
|                                 | No COVID-19 (n = 724)           | COVID-19 + (n = 14)              |
|                                 | P                               | P                               |
| DEMOGRAPHICS                    |                                 |                                 |
| Age group                       |                                 |                                 |
| Newly born                      | 359 (27.0)                      | 61 (10.9)                       |
| Neoponates                      | 430 (32.4)                      | 153 (27.4)                      |
| >1 month to 8 years             | 285 (21.5)                      | 160 (28.7)                      |
| >8 to <18 years                 | 254 (19.1)                      | 184 (33.0)                      |
| Female sex                      | 592 (44.6)                      | 260 (46.6)                      |
| Race                            |                                 |                                 |
| White                           | 599 (45.1)                      | 255 (45.7)                      |
| Black                           | 337 (25.4)                      | 132 (23.7)                      |
| Other                           | 70 (5.3)                        | 37 (6.6)                        |
| Unknown                         | 322 (24.3)                      | 134 (24.0)                      |
| Hispanic ethnicity              | 216 (16.3)                      | 99 (17.7)                       |
| CARDCIAL ARREST FACTORS         |                                 |                                 |
| Location of arrest              |                                 |                                 |
| Intensive care unit             | 1028 (77.4)                     | 379 (67.9)                      |
| Telemetry unit                  | 7 (0.5)                         | 6 (1.1)                         |
| Non-monitored hospital unit     | 54 (4.1)                        | 33 (5.9)                        |
| Emergency room                  | 116 (8.7)                       | 84 (15.1)                       |
| Procedural area                 | 111 (8.4)                       | 52 (9.3)                        |
| Other                           | 12 (0.9)                        | 4 (0.7)                         |
| Time of Arrest                  |                                 |                                 |
| Night (11 PM to 6:59 AM)        | 371 (28.1)                      | 159 (28.6)                      |
| Weekend                         | 378 (28.5)                      | 167 (29.9)                      |
| Initial Cardiac Arrest Rhythm   |                                 |                                 |
| Asystole                        | 193 (14.5)                      | 186 (33.3)                      |
| Pulseless electrical activity   | 338 (25.5)                      | 314 (56.3)                      |
| Ventricular fibrillation        | 21 (1.6)                        | 21 (3.8)                        |
| Pulseless ventricular tachycardy| 38 (2.9)                        | 37 (6.6)                        |
| Bradycardia                     | 738 (55.6)                      | 0 (0.0)                         |
| PRE-EXISTING CONDITIONS         |                                 |                                 |
| Cyanotic congenital heart disease| 228 (17.2)                      | 88 (15.8)                       |
| Heart failure this admission    | 48 (3.6)                        | 20 (3.6)                        |
| Heart failure prior to admission| 41 (3.1)                        | 33 (6.8)                        |
| Myocardial infarction this admission| 4 (0.3)          | 3 (0.5)                        |
| Myocardial infarction prior to admission| 3 (0.2)   | 1 (0.2)                        |
| Hypertension                    | 399 (30.1)                      | 175 (31.4)                      |
| Respiratory insufficiency       | 947 (71.3)                      | 366 (65.6)                      |
| Renal insufficiency             | 143 (10.8)                      | 68 (12.2)                       |
| Hepatic insufficiency           | 50 (3.8)                        | 31 (5.6)                        |
| Metabolic or electrolyte abnormality| 332 (25.0)                      | 146 (26.2)                      |
| Diabetes mellitus               | 24 (1.8)                        | 17 (3.1)                        |
| Baseline depression in CNS function| 212 (16.0)                      | 101 (18.1)                      |
| Acute stroke                    | 18 (1.4)                        | 9 (1.6)                         |
| Acute CNS non-stroke event      | 146 (11.0)                      | 77 (13.8)                       |
| Pneumonia                       | 62 (4.7)                        | 24 (4.3)                        |
| Sepsis                          | 189 (14.2)                      | 65 (11.7)                       |
| Metastatic or hemotologic malignancy| 46 (3.5)                       | 33 (5.9)                        |
| INTERVENTIONS IN PLACE AT TIME OF ARREST |           |                                 |
| Continuous intravenous vasopressor | 537 (40.5)                      | 316 (56.7)                      |
| Assisted or Mechanical ventilation| 919 (69.3)                      | 378 (68.0)                      |
| Hemodialysis                    | 40 (3.0)                        | 22 (3.9)                        |

*Comparisons made with chi-square statistics or Fisher's exact test.

Abbreviation: CNS, central nervous system.
Table 2 – Association between COVID-19 infection and survival outcomes.

| Survival to Discharge | COVID + | COVID – | Adjusted RR (95% CI) | P     | Interaction P |
|-----------------------|---------|---------|----------------------|-------|---------------|
| Overall†              | 18/46 (39.1) | 576/1282 (44.9) | 1.14 (0.55, 2.36) | 0.73  | 0.96          |
| Pulseless IHCA†       | 10/32 (31.3) | 208/558 (37.3) | 1.03 (0.53, 2.00) | 0.93  |               |
| Bradycardia†          | 8/14 (57.1) | 368/724 (50.8) | 1.05 (0.52, 2.14) | 0.89  |               |
| ROSC                  | 31/46 (67.4) | 986/1282 (76.9) | 0.87 (0.43, 1.77) | 0.71  | 0.26          |
| Pulseless IHCA†       | 21/32 (65.6) | 389/558 (69.7) | 0.95 (0.60, 1.50) | 0.83  |               |
| Bradycardia†          | 10/14 (71.4) | 597/724 (82.5) | 0.86 (0.46, 1.62) | 0.64  |               |

Abbreviations: CI, confidence interval; IHCA, in-hospital cardiac arrest; RR, risk ratio; ROSC, return of spontaneous circulation for ≥20 minutes.
† Models for the overall cohort adjusted for COVID-19 status, initial rhythm, location of arrest, age group, pneumonia, sepsis, hypotension, and renal insufficiency.
‡ Models for IHCA adjusted for: COVID-19 status, initial rhythm, location of arrest, pneumonia, sepsis, and hypotension.
§ Model for bradycardia adjusted for: COVID-19 status, location of arrest, hypotension, and sepsis.

Conclusions

In a large multicenter national registry of CPR events, sCOVID-19 infection status was not associated with lower rates of ROSC or survival to hospital discharge in pediatric patients undergoing CPR.

Conflicts of Interest and Disclosures

- Dr. El-Zein is currently supported by the National Heart, Lung and Blood Institutes of Health under Award Number T32H110837. The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the National Institutes of Health.
- “The Get With The Guidelines® programs are provided by the American Heart Association.” Hospitals participating in the registry submit clinical information regarding the medical history, hospital care, and outcomes of consecutive patients hospitalized for cardiac arrest using an online, interactive case report form and Patient Management Tool™ (IQVIA, Parsippany, New Jersey). IQVIA (Parsippany, New Jersey) serves as the data collection (through their Patient Management Tool – PMT) and coordination center for the American Heart Association/American Stroke Association Get With The Guidelines® programs. The University of Pennsylvania serves as the data analytic center and has an agreement to prepare the data for research purposes.

Contributors’ statement

Rayan El-Zein and Paul S. Chan conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Maya L. Chan carried out the analyses. Lillian Su critically reviewed the manuscript.

Members of the Pediatric Research Task Force include:

Anne-Marie Guerguerian MD PhD FRCPC; Dianne Atkins MD; Elizabeth E. Foglia MD MSCE; Ericka Fink MD; Javier J. Lasa MD; Rayan El-Zein MD; Paul S. Chan MD; Maya L. Chan MD; Maya L. Chan MD.
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