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Resuscitation Characteristics and Outcomes in Suspected Drug Overdose-Related Out-of-Hospital Cardiac Arrest

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Abstract

Introduction—We sought to compare characteristics of emergency medical services-treated out-of-hospital cardiac arrests resulting from suspected drug overdose with non-overdose cases and test the relationship between suspected overdose and survival to hospital discharge.

Methods—Data from emergency medical services-treated, non-traumatic out-of-hospital cardiac arrests from 2006–2008 and late 2009–2011 were obtained from 4 EMS agencies in the Pittsburgh, Pennsylvania metropolitan area. Case definition for suspected drug overdose was naloxone administration, indication on the patient care report and/or indication by a review of hospital records. Resuscitation parameters included chest compression fraction, rate, and depth and the administration of resuscitation drugs. Demographic and outcome variables compared by suspected overdose status included age, sex, and survival to hospital discharge.

Results—From 2,342 treated out-of-hospital cardiac arrests, 180 were suspected overdose cases (7.7%) and were compared to 2,162 non-overdose cases. Suspected overdose cases were significantly younger (45 vs. 65, $p < 0.001$), less likely to be to be witnessed by a bystander (29% vs. 41%, $p < 0.005$), and had a higher rate of survival to hospital discharge (19% vs. 12%, $p = 0.014$) than non-overdoses. Suspected overdose cases had a higher overall chest compression fraction (0.69 vs. 0.67, $p = 0.018$) and higher probability of adrenaline, sodium bicarbonate, and atropine administration ($p < 0.001$). Suspected overdose status was predictive of survival to hospital discharge when controlling for other variables ($p < 0.001$).

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Conflicts of Interest
The authors report no conflicts of interest regarding this work.

Conflict of Interest Statement:
The authors, Allison C. Koller, David D. Salcido, Clifton W. Callaway, and James J. Menegazzi, report no conflicts of interest regarding this manuscript.

Conclusion—Patients with suspected overdose-related out-of-hospital cardiac arrest were younger, received different resuscitative care, and survived more often than non-overdose cases.

Introduction

Out-of-hospital cardiac arrest (OHCA) from suspected drug overdose (OD) is a significant public health issue in the United States and abroad. Published incidence rates vary geographically between 2.7 and 29.4% of all non-traumatic, emergency medical services (EMS)-treated OHCA.[1–5] In the developed world, the most common etiology of non-traumatic OHCA is cardiac, primarily myocardial infarction due to atherosclerosis and coronary artery disease.[6] Suspected OD-OHCA then presents a unique subset of cardiac arrests that results from the misuse of a variety of illicit, legal, and/or prescribed agents. While the literature is limited on the topic, the most common agents implicated in suspected OD-OHCA are opioids, cocaine, and alcohol,[3] with opioids accounting for 75.2% of all drug-related deaths in 2010 in the United States.[7] Opioids are also the most often implicated substance in cases of polypharmaceutical overdose.[7] Other agents commonly abused include antidepressants, antiepileptics, antihistamines, barbiturates, and benzodiazepines. [3, 7]

Despite clear differences in the etiology of suspected OD and non-OD OHCA, the International Liaison Committee on Resuscitation guidelines published in 2010 do not specify different treatments for suspected OD-OHCA patients during resuscitation, and state that there is no evidence promoting the intra-arrest administration of the opioid antagonist naloxone.[8] Data are required to determine if alternative management strategies might be beneficial for suspected OD-OHCA.

In the present study, we describe the characteristics of the subset of OHCA cases attributed to suspected OD in a distinct geographic area. Second, we compared patient and treatment characteristics between suspected OD-OHCA and non-OD OHCA cases. Lastly, we investigated the relationship between suspected OD status and survival to hospital discharge, adjusting for other characteristics.

Methods

We obtained approval from the Institutional Review Board of the University of Pittsburgh prior to commencing this retrospective study. Case data from EMS-treated OHCAs occurring from 2006 to late 2008 and late 2009 to 2011 were obtained from the Pittsburgh site of the Resuscitation Outcomes Consortium (ROC), a multicenter clinical research network with ten sites across the United States and Canada. The catchment area for this study included a population of approximately 940,000 people, with an annual incidence of OHCA estimated to be 105.1 per 100,000, as of 2008. This region encompassed the service areas of 4 EMS agencies, all of which provided advanced life support (ALS) care.[9] We excluded cases identified as “dead on arrival” (DOA) by EMS, as well as cases from a period spanning late 2008 to late 2009, during the multisite ROC PRIMED clinical trial for which the data were embargoed.[10]

Available patient and treatment data sources included prehospital patient care reports (PCRs) written by paramedics, electronic ECG files from defibrillator monitors, and select

data elements from hospital records. Cardiopulmonary resuscitation (CPR) process parameters including chest compression fraction (CCF), rate, and depth were abstracted from defibrillator downloads by data abstractors for up to the first 20 minutes of each resuscitation event. Frequency of shock delivery, as well as the administration of resuscitation drugs including adrenaline (epinephrine), sodium bicarbonate, lidocaine, atropine, and amiodarone were abstracted from PCRs and defibrillator downloads. Drug administration for ALS drugs was coded as "administered ever" for each drug.

We identified suspected OD cases by three criteria: 1) the administration of at least one dose of naloxone during prehospital resuscitation, and 2) paramedic indication of suspected overdose in the PCR. In the latter case, explicit mention of drugs intended for medicinal or recreational use, drug paraphernalia, or witness accounts of drug use leading to cardiac arrest were necessary for establishing suspected OD status. Pesticides and other environmental poisonings were not included in the suspected OD subset. Specific agents contributing to OHCA were not identifiable in all cases, however for consistency with existing research,[1] we attempted to limit the study to illicit and prescription drugs and excluded cases that only mentioned alcohol. The third method of suspected OD identification utilized in-hospital confirmation of drug use provided by data abstractors using select data elements from hospital records. ROC data abstractors could indicate the "suspected cause of arrest" was drug overdose (prescribed or illicit) after review of in-hospital records, however, this data point was only available for OHCA patients who were admitted to the hospital; this did not yield any information pertaining to patients whose resuscitation was terminated in the out-of-hospital setting. Furthermore, demographic, condition and circumstantial variables included age, sex, EMS- and bystander-witnessed status, return of spontaneous circulation, survival to hospital admission, and survival to hospital discharge.

Clinical characteristics were compared between suspected OD and non-OD cases with two-tailed comparison of proportions and t-tests. The effect of suspected OD status and time on CCF was tested with a simple generalized estimating equations (GEE) model. To assess the independent relationship between suspected OD status and survival while adjusting for demographic and clinical covariates, a multivariable logistic regression model was constructed, and adjusted odds ratios (OR) were reported. Suspected OD status was forced into the logistic model as a key variable, and other variables were included in the model if they had significant univariate relationships with suspected OD status. All statistical calculations were conducted with Stata 11 (StataCorp, College Station, TX) using an alpha level of 0.05.

Results

For the period between 2006 and 2011, a total of 2,342 OHCA cases were available for inclusion in this study. Of these, 180 cases (7.7%) were identified as suspected OD-OHCA, leaving 2,162 non-OD OHCA. Naloxone administration was the identifying factor for 168 (93.3%) cases. Fifty-one cases (28.3%) included in our suspected OD group had an indication of suspected OD by paramedics in the out-of-hospital setting; 39 (21.7%) were

confirmed as an overdose in the hospital (see Figure 1). There was extremely limited data on DOA cases and we could not confidently compare such cases to those in our study cohort.

Table 1 summarizes characteristics and outcomes by suspected OD status. Suspected OD-OHCA cases were younger and less-often bystander witnessed than non-OD cases. Sex and EMS witnessed status did not differ by suspected OD status. Suspected OD cases were more likely than non-ODs to survive to hospital discharge (OR: 1.82, 95% CI: 1.12–2.94, p = 0.015).

Table 2 summarizes CPR process parameters. Overall chest compression rate and depths did not differ between suspected OD and non-OD cases. Average CCF was higher in the suspected OD-OHCA group than the non-OD group across the entire available resuscitation period. However CCF did not differ between groups over the first 5 minutes of the resuscitation. The time course of CCF is shown in Figure 2. A GEE model of CCF containing time and suspected OD status yielded no significant relationship between suspected OD status and CCF across the available resuscitation period, but did show a significant relationship between time and CCF ($p < 0.001$).

Table 3 summarizes the rates of key drug interventions, as well as rescue shocks, by suspected OD status. The proportion of cases shocked and average number of shocks delivered did not differ between groups. However, rates of administration of adrenaline, bicarbonate, and atropine were higher in suspected OD cases than non-ODs.

A multivariable logistic regression model testing for an independent effect of suspected OD status on survival to hospital discharge is shown in Table 4. Suspected OD status and an initial VF/VT rhythm had independent direct associations with survival. Adrenaline and atropine administration had independent inverse associations with survival.

Discussion

We found that the treatment and outcomes of suspected OD-OHCA differed from those of non-OD OHCA. Demographic features of non-OD and suspected OD cases also differed. We cannot determine whether these differences in treatment or demographic characteristics are related to differences in outcome. However, these data do support the idea that treatment might be tailored to the cause of cardiac arrest in an effort to improve outcomes.

We encountered difficulty in ascertainment of suspected OD as a cause of cardiac arrest. Autopsy is rare for OHCA, and only a fraction cases reach the hospital for further testing. We relied on either naloxone administration or clear description of circumstantial evidence in the PCR to identify a suspected OD. Clear descriptions are also rare, and most (93%) of the cases were identified by naloxone administration. Naloxone during cardiac arrest is not part of any regional protocol, and all of these administrations are deviations from recommended practice. There may be other cases in which paramedics suspected OD, but did not deviate from protocol to administer naloxone. Therefore, it is impossible to be certain whether the actual number of OD cases is larger or smaller than the reported number. However, the use of naloxone as a proxy indicator of suspected OD has been supported in the literature.[11] It is likely that the current sample of 180 suspected OD-OHCA cases

represent situations in which the treating paramedics at least considered opioid OD as a possible contributor to arrest.

Our study provides additional description of suspected OD-OHCA, a historically understudied phenomenon. A handful of previous studies provide characteristics of patients presenting with this general etiology of OHCA. When compared to the 2004 study by Paredes et al., our suspected OD-OHCA patients are similar in age, and relatively close in distribution of sexes (73% male versus 65%). Our suspected OD-OHCA cases had higher survival (19%), compared to both Paredes's study (12.9%) and a 2007 study by Hess et al. (11.1%). Additionally, Paredes found a much lower rate of first EMS assessed OHCA ECG rhythm of VF/VT (6%),[3] compared to our own estimate of 15.6%.

This study had several limitations. First, embargoed data resulting in exclusion of a large period of time from the middle of the study period limits a complete epidemiological estimate of the incidence of suspected OD-OHCA. However, there is no reason to suspect that cases differed during that period were not comparable to the cases captured during the period of our study. Second, when ascertaining suspected OD status, we relied on a combination of evidence of naloxone administration and PCR review for indication of direct or circumstantial evidence indicating suspected OD, which has the limitations discussed above. Moreover, we are unable to state with certainty which drugs were utilized in each arrest, as this information is difficult to obtain in the prehospital environment, and toxicology reports were not available for our review. Lastly, as this was a retrospective study utilizing records and a surveillance network that were conceived before our study, we were unable to capture several data points that might have clarified our findings, including toxicological screens of patients post-resuscitation or at autopsy.

Conclusion

Suspected OD-OHCA patients were treated differently than non-OD cases to a limited degree, particularly in drug administration and one parameter of CPR. Suspected OD-OHCAs were also more likely to be younger and to survive to hospital discharge than non-OD OHCAs.

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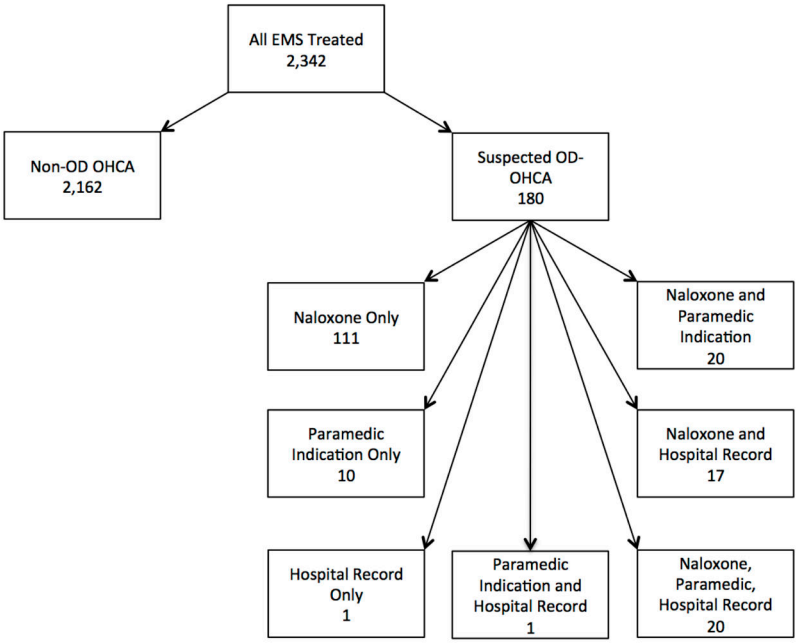

Figure 1.

Consort Diagram

Abbreviations:

EMS: Emergency Medical Services; Non-OD OHCA: Non-Overdose Out-of-Hospital Cardiac Arrest; OD-OHCA: Suspected Overdose Out-of-Hospital Cardiac Arrest

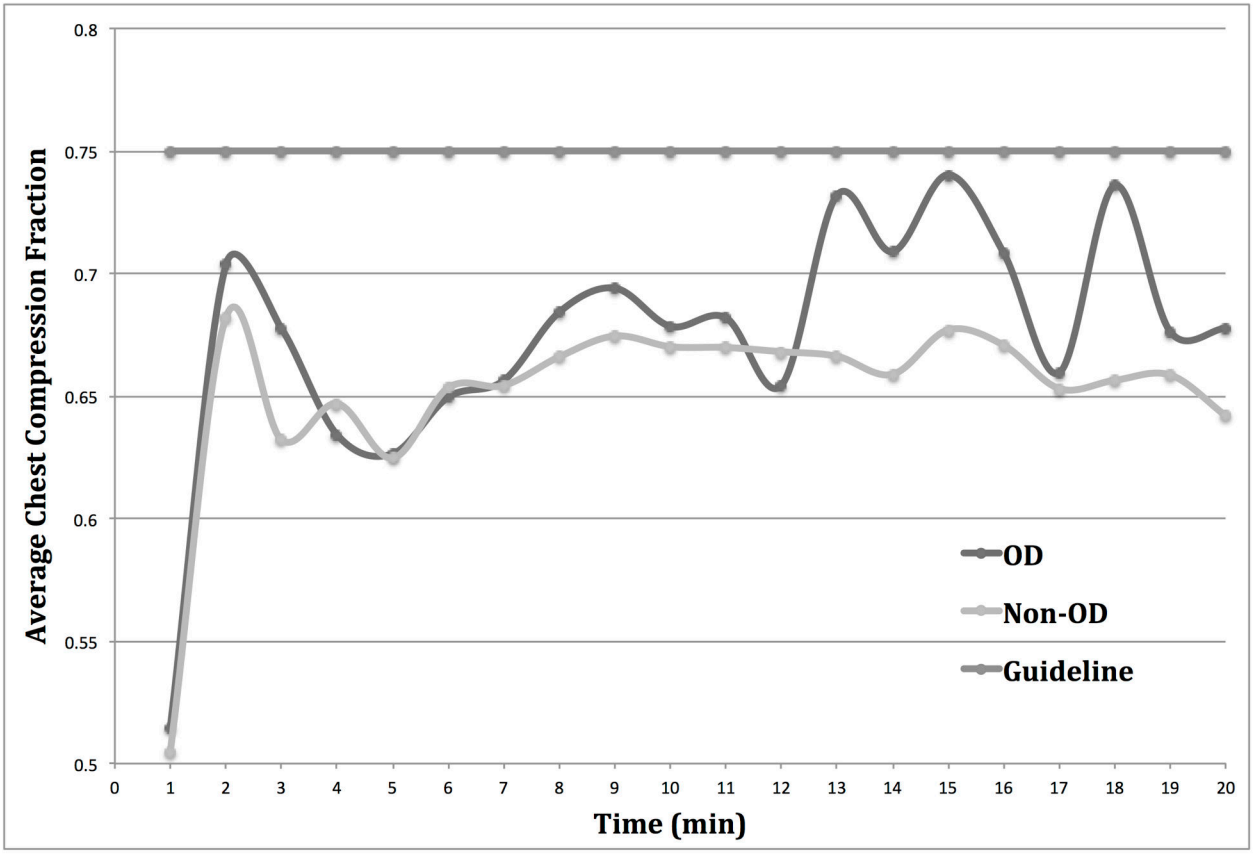

Figure 2.

Average Chest Compression Fraction of OD vs. Non-OD Cases

Abbreviations:

Non-OD: Non-Overdose Out-of-Hospital Cardiac Arrest; OD: Suspected Overdose Out-of-Hospital Cardiac Arrest

Table 1

Characteristics and Outcomes Stratified by OD Status

Variable	Overall	OD	Non-OD	p-value
Age, y mean (SD)	63.6 (19.6)	44.8 (14.7)	65.1 (19.1)	< 0.001
Sex, % (SE)	60.0 (1.0)	65.4 (3.6)	59.6 (1.1)	0.130
EMS Witnessed, % (SE)	9.3 (0.7)	6.7 (1.9)	9.5 (0.7)	0.207
Bystander Witnessed, % (SE)	51.3 (1.2)	48.4 (4.4)	51.5 (1.2)	0.508
Bystander Resuscitation, % (SE)	51.3 (1.2)	48.4 (4.4)	51.5 (1.2)	0.508
Public Location, % (SE)	14.1 (0.7)	17.2 (2.8)	13.8 (0.7)	0.210
VF/VT First OHCA ECG Rhythm, % (SE)	13.1 (0.7)	15.6 (2.7)	12.9 (0.7)	0.302
ROSC, % (SE)	26.3 (0.9)	25.0 (3.2)	26.4 (0.9)	0.689
Survival to Hospital Admission, % (SE)	31.3 (1.3)	34.2 (4.4)	31.1 (1.3)	0.486
Survival to Hospital Discharge, % (SE)	11.9 (0.8)	18.9 (3.5)	11.3 (0.8)	0.014

Abbreviations:

ECG: Electrocardiogram; EMS: Emergency Medical Service; Non-OD: Non-Overdose Out-of-Hospital Cardiac Arrest; OD: Suspected Overdose Out-of-Hospital Cardiac Arrest; OHCA: Out-of-Hospital Cardiac Arrest; SD: Standard Deviation; SE: Standard Error; VF/VT: Ventricular Fibrillation/Ventricular Tachycardia

Table 2

CPR Process Parameters Stratified by OD Status

Process Measures	Overall	OD	Non-OD	p-value
Compression Rate, Case Average (SD)	78.7 (29.8)	80.7 (27.8)	78.5 (30.1)	0.402
Compression Rate, First 5 min Average (SD)	79.3 (35.3)	80.5 (35.1)	79.2 (35.3)	0.661
Compression Depth, Case Average (SD)	37.4 (8.4)	38.6 (7.6)	37.3 (8,5)	0.109
Compression Depth, First 5 min Average (SD)	37.9 (9.7)	38.6 (8.5)	37.8 (9.8)	0.430
Compression Fraction, Case Average (SD)	67.1 (12.3)	69.4 (10.6)	66.9 (12.5)	0.018
Compression Fraction, First 5 min Average (SD)	65.4 (14.1)	65.8 (13.1)	65.3 (14.2)	0.666

Abbreviations:

Non-OD: Non-Overdose Out-of-Hospital Cardiac Arrest; OD: Suspected Overdose Out-of-Hospital Cardiac Arrest; SD: Standard Deviation

Table 3

Prehospital Interventions Stratified by OD Status

Intervention	Overall	OD	Non-OD	p-value
Shocked, % (SE)	31.6 (1.0)	33.9 (3.5)	31.4 (1.0)	0.483
Shocks, mean (SD)	3.1 (2.5)	2.9 (2.6)	3.1 (2.5)	0.505
Adrenaline, % (SE)	75.4 (0.9)	85.6 (2.6)	74.3 (1.1)	<0.001
Bicarbonate, % (SE)	31.1 (1.1)	52.2 (3.7)	28.8 (1.1)	<0.001
Amiodarone, % (SE)	5.4 (0.5)	5.6 (1.7)	5.4 (0.5)	0.925
Atropine, % (SE)	68.7 (1.1)	78.9 (3.0)	67.6 (1.1)	<0.005

Abbreviations:

Non-OD: Non-Overdose Out-of-Hospital Cardiac Arrest; OD: Suspected Overdose Out-of-Hospital Cardiac Arrest; SD: Standard Deviation; SE: Standard Error

Table 4

Multivariable Logistic Regression with Outcomes of Survival to Hospital Discharge

Predictor	OR	95% CI	p-value
OD Status	3.89	1.91–7.92	<0.001
Age	1.00	0.99–1.01	0.785
Sex	0.67	0.42–1.07	0.095
Bystander Witnessed	1.09	0.78–1.53	0.600
VF/VT First OHCA ECG Rhythm	6.87	4.10–11.49	<0.001
Adrenaline	0.18	0.09–0.34	<0.001
Bicarbonate	0.83	0.45–1.55	0.565
Atropine	0.19	0.10–0.36	<0.001

Abbreviations:

95% CI: 95% Confidence Interval; ECG: Electrocardiogram; Non-OD: Non-Overdose Out-of-Hospital Cardiac Arrest; OD: Suspected Overdose Out-of-Hospital Cardiac Arrest; OHCA: Out-of-Hospital Cardiac Arrest; OR: Odds Ratio; VF/VT: Ventricular Fibrillation/Ventricular Tachycardia