Title

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Publication Date

2021-11-01

DOI

10.1016/j.ajem.2021.05.073

Peer reviewed

American Journal of Emergency Medicine 49 (2021) 195–199

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Prehospital, post-ROSC blood pressure and associated neurologic outcome

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ARTICLE INFO

Article history:
Received 2 January 2021
Received in revised form 23 May 2021
Accepted 27 May 2021

Keywords:
Ventricular fibrillation/etiology
Hemodynamic goals
Age factors
Body temperature
Cardiopulmonary resuscitation
Cardiotonic agents/therapeutic use
Comorbidity
Databases
Factual
Emergency medical services/EMS
Heart arrest/mortality
Heart arrest/therapy
Humans
Hypotension/mortality
Hypothermia
Induced/methods*
Out-of-hospital cardiac arrest/complications
Out-of-hospital cardiac arrest/mortality
Out-of-hospital cardiac arrest/therapy*

ABSTRACT

Objective: To investigate the relationship between hypotension and neurologic outcome in adults with return of spontaneous circulation after out-of-hospital cardiac arrest.
Methods: Blood pressure and medication data were extracted from adult patients who had ROSC after OHCA in Alameda County and matched with neurologic outcome using the CARES database from January 1, 2018 through July 1, 2019. We used univariate logistic regression with $p \leq 0.2$ followed by multivariate logistic regression and reported an odds ratio with 95% confidence intervals.
Results: Among the 781 adult patients who had ROSC after OHCA, 107 (13.7%) were noted to be hypotensive and 61 (57% of the hypotensive group) received vasopressors. Patients with a final prehospital blood pressure recording of <90 mmHg were more likely to have a poor neurologic outcome (adjusted odds ratio 2.13, adj $p = 0.048$). About twice as many patients who were not hypotensive had a good neurologic outcome compared to hypotensive patients who had a good neurologic outcome (23% to 10.3%). Additionally, patients who were hypotensive and did not receive vasopressors had a similar neurologic outcome compared to patients who did receive vasopressors.
Conclusion: Prehospital post-ROSC hypotension was associated with worse neurologic outcome and giving hypotensive patients vasopressors may not improve neurologic outcome in the prehospital setting.

1. Introduction

More than 350,000 patients each year suffer out-of-hospital cardiac arrest (OHCA) in the United States, and approximately 20–30% achieve return of spontaneous circulation (ROSC) [1]. About 60–70% of those patients admitted to the hospital after ROSC end up dying in the hospital [2]. Those who survive to discharge can be plagued by neurologic sequelae. Over the past decade, there has been considerable research in optimizing the prehospital use of Advanced Cardiac Life Support (ACLS) and more recently on the hospital portion of post cardiac arrest care. The prehospital management of ROSC patients has received less attention and is quite variable [3].

While cardiac arrest care is well algorithmized, post-ROSC care in the field is often not. Prehospital, post-ROSC care typically includes monitoring ventilations with special attention to avoid hyperventilation, monitoring end-tidal CO_2 waveform, managing hypotension with intravenous fluids and/or vasopressors, and performing a 12-lead EKG to recognize ST segment elevated myocardial infarctions. The use of prehospital targeted temperature management has not been demonstrated to be beneficial in a system routinely performing in-hospital therapeutic hypothermia [4].

Minimizing end-organ damage includes preventing and treating hypotension and shock. In-hospital, post-ROSC hypotension, especially when vasopressors are used, is associated with worse neurologic outcome and increased mortality for adults [5-8] and children [9] compared to those who are not hypotensive. Hypotension is usually defined as SBP < 90 mmHg or mean arterial pressure (MAP) <65 mmHg, although some studies suggest cerebral autoregulation is

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https://doi.org/10.1016/j.ajem.2021.05.073
0735-6757/

impaired after ROSC and a higher MAP of 80–100 may be needed for adequate cerebral profusion. [10-12].

Many studies comparing neurologic outcome and hypotension do not examine prehospital hypotension, but rather hypotension at time of ICU admission or during ED stay. One study looked at hypotension on ED arrival and is therefore reflective of the patient's prehospital course. Hypotension was associated with lower odds of survival to hospital discharge for patients with a shockable rhythm [13]. After adjusting for other variables, there did not seem to be a significant association for hypotensive patients with non-shockable rhythms and survival. Neurologic outcome was not mentioned. There was a French study that found prehospital SBP's of 100–130 mmHg correlated with a better neurologic outcome [14], but there are few, if any, studies examining the effect of prehospital hypotension treated with vasopressors on neurologic outcome.

A 2018 study of 263 patients who had ROSC after OHCA showed that patients who died in the hospital had lower mean arterial pressures (MAP) than patients who were discharged alive, but there was no difference in blood pressures in patients who survived to discharge and had a good neurologic outcome and those who had a poor neurologic outcome. Authors in this abstract concluded early recovery from hypotension had a higher probability of good neurologic outcome [15]. It remains unclear whether early recovery from hypotension because of vasopressors or because of a healthier cardiovascular system in general is responsible for the better neurologic outcome. It also remains unclear whether vasopressors are important in the prehospital environment, or if starting them after the patient arrives to the ED is equivalent. A paper examining push-dose epinephrine during critical care transport found that after administration, hypotension was resolved in 55 of 94 (58%) instances and the median increase in MAP was 13 mmHg [16]. Their study did not focus on the clinical outcome of the patient, however, so it's unclear if improvement in blood pressure was correlated with neurologic outcome. Additionally, as this was critical care transport, patients were alive and had some level of care performed prior to their EMS care during transport.

While it studied resuscitation-dose epinephrine during the cardiac arrest, the PARAMEDIC-2 trial did show increased rates of survival at 30 days with increased use of epinephrine, but no improvement in neurologic outcome [17]. Again, while the epinephrine was not for treatment of hypotension, but rather cardiac arrest, the results highlight the fact that epinephrine and increased blood pressure may not lead to a favorable neurologic outcome.

Many EMS agencies have protocols for treating hypotension, including fluids and vasopressors like dopamine, epinephrine and more recently push dose epinephrine. These treatments are potentially underutilized due to lack of protocol, education or recognition of the opportunity, however. Additionally, EMS crews have many tasks to complete for a patient after ROSC, including packaging and loading the patient for transport, loading equipment, taking vital signs, obtaining an EKG, and giving a hospital report. These tasks may be prioritized over treating hypotension when the crew is only a few minutes away from the hospital with the patient.

This study compares outcomes of patients who have hypotension after ROSC versus those who are not hypotensive (either normotensive or hypertensive) and their neurologic outcome, and to see if vasopressors could potentially maximize a patient's chance at meaningful survival.

2. Methods

Alameda County is a 737-mile^2, urban/suburban county in Northern California with a population of 1.67 million. The Alameda County Emergency Medical Services Agency prescribes county wide response, treatment and transport protocols, and ongoing quality oversight and improvement strategies. The paramedic-staffed first response engines and transport ambulances respond to 160,000 EMS calls and transport 115,000 patients each year. This system responds to and initiates resuscitation on over 1100 patients with non-traumatic cardiac arrest each year. All cardiac arrest patients with ROSC at any time are transported to the closest Cardiac Arrest/STEMI center. Those without prehospital ROSC who are transported can be sent to the closest of 12 adult hospitals or terminated in the field.

The University of California San Francisco (UCSF) Committee on Human Research determined that Institutional Review Board (IRB) oversight was not required for this study because the data were extracted from a performance improvement data set with no identifiable personal information.

Prehospital electronic patient care records were associated with outcomes by matching incident numbers between the record and data in the Cardiac Arrest Registry to Enhance Survival (CARES) database. The CARES database provided data for non-traumatic out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation and achieved ROSC in the care of EMS personnel from January 1, 2018 through July 1, 2019. All data were deidentified prior to review and analysis. These data include demographics, initial rhythm, witnessed status, presence of bystander CPR, EMS response times, advanced airway use, advanced cardiovascular life support (ACLS) drug use, ITD (ResQPOD™ ITD-10, Advanced Circulatory Systems Inc., Roseville, MN) use, mechanical CPR device use (LUCAS 2™, Physiocontrol Corporation, Redmond WA, or AutoPulse™, Zoll Medical, Chelmsford MA), return of spontaneous circulation (ROSC) at any time, time from EMS CPR to ROSC, admission to the hospital, in hospital targeted temperature management, survival to hospital discharge, and CPC score at hospital discharge. The LUCAS device was programmed to a compression-ventilation ratio of 30:2 during BLS care and converted to continuous compressions once an advanced airway was achieved.

During the study period, resuscitations were performed according to the American Heart Association basic and advanced life support guidelines and included the use of epinephrine, and amiodarone when indicated, the option of an endotracheal intubation (ETT) or supraglottic

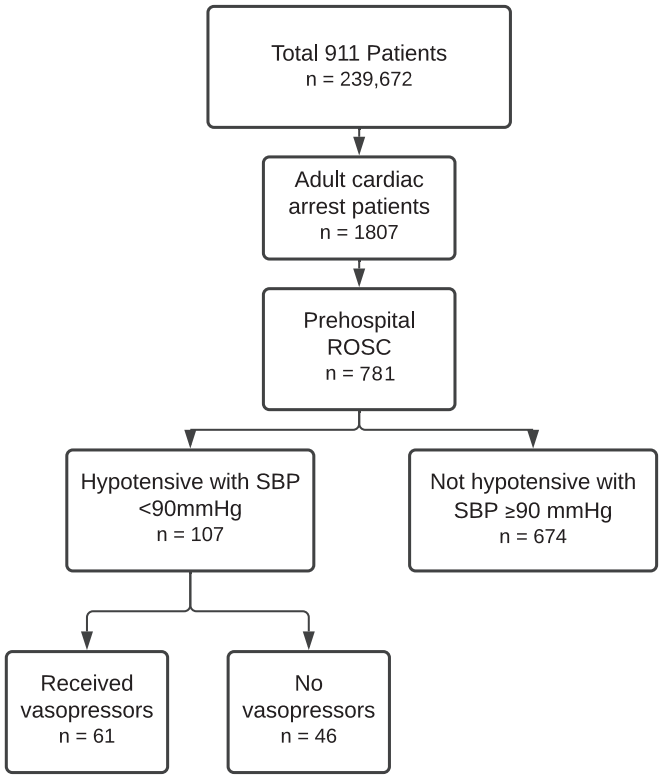

Fig. 1. Population description.

airway (King LTD™ tube) for advanced airway management, intravenous or intraosseous access, and the use of quantitative capnography. ROSC care was performed according to our protocol, listed in Supplement 1. First responder vehicles were outfitted with a mechanical CPR device. Dopamine was the standard and sole vasopressor until January 2018, when the protocol was changed to push-dose epinephrine as the new, sole vasopressor choice. Only transporting EMS agencies were examined because they were most likely to be the ones caring for the patient with ROSC and to avoid duplication of data, as different responding agencies occasionally both document the same intervention on different patient care records.

Patients who experienced prehospital ROSC were included in our study. The only blood pressures available from our patient care record database were the first and last blood pressure recorded. Patients were excluded if they did not have a final blood pressure reading or if it was zero. Patients were then grouped into one of three categories – hypotensive as defined by final blood pressure reading with systolic between 1 and 89 mmHg, not hypotensive (90 mmHg or greater) or received vasopressors. Final blood pressure was used for categorization instead of first recorded blood pressure, because the majority of initial blood pressures were recorded as 0 mmHg to reflect the fact that the patient was in cardiac arrest, as opposed to a blood pressure taken immediately after ROSC. The initial blood pressure was therefore not a reliable measure of blood pressure after ROSC, whereas final BP was always after ROSC. Because there is no indication for dopamine or push-dose epinephrine other than hypotension in our protocols, patients who received vasopressors were assumed to be hypotensive, regardless of recorded blood pressure reading. We then attempted to look for an association between blood pressure after ROSC and final neurologic outcome. We used univariate logistic regression with $p \leq 0.2$ followed by multivariate logistic regression and reported an odds ratio with 95% confidence intervals. Neurologic outcome at the time of discharge was measured in terms of cerebral perfusion category, where 1 and 2 were considered "good" neurologic outcome and 3–5 were considered "poor."

3. Results

Of the 1807 patients who were in cardiac arrest and received CPR, 781 patients achieved prehospital ROSC (Fig. 1). After controlling for time to first responder arrival, age, sex, race, initial cardiac rhythm, whether or not the arrest was witnessed, bystander CPR, bystander AED use, arrest after or before first responder arrival, mechanical CPR and airway, patients who were hypotensive were found to have an increased association with poor neurologic outcome (adjusted odds ratio 2.13, adj $p = 0.048$). The 155 (23%) of 674 patients who were

Table 1
Prehospital data and neurologic outcome.

	n (%) or median (IQR)	n (%) or median (IQR)				
	171 (20.3)	671 (79.7)				
	Good Outcome/Moderate Disability	Poor Outcome/Non-Survival	Unadjusted Odds Ratio	Adjusted Odds Ratios	*p*-value	adj. p-val
Time to First Responder Arrival (min)	6 (4–8)	6 (4–8)	0.99 (0.93–1.04)	–	0.69	
Age	62 (51–71)	71 (60–83)	0.97 (0.96–0.98)	0.97 (0.96–0.98)	<0.001	<0.001
Female	58 (16.4)	296 (83.6)	*Ref*			
Male	113 (23.2)	375 (76.8)	1.54 (1.08–2.19)	–	0.016	–
Race = White	67 (26.8)	183 (73.2)	*Ref*			
Race = Asian	14 (11.4)	109 (88.6)	0.35 (0.19–0.65)	–	<0.01	–
Race = Black	33 (22.0)	117 (78.0)	0.77 (0.48–1.24)	–	0.42	–
Race = Latino	14 (24.6)	43 (75.4)	0.89 (0.46–1.73)	–	0.26	–
Race = Other	43 (16.4)	219 (83.6)	0.54 (0.35–0.83)	–	0.20	–
Systolic (90 + mmHg)	155 (23.0)	519 (77.0)	*Ref*			
Systolic (1–89 mmHg)	11 (10.3)	96 (89.7)	0.38 (0.20–0.73)	–	0.14	–
Dopamine or Push Dose Epi	5 (8.2)	56 (91.8)	0.30 (0.12–0.76)	–	0.37	–
Non-Cardiac	21 (12.9)	142 (87.1)	*Ref*			
Cardiac	150 (22.1)	529 (77.9)	1.92 (1.17–3.14)	–	0.01	–
Any Other Initial Rhythm	75 (11.7)	567 (88.3)	*Ref*			
Ventricular Fibrillation or Tachycardia	96 (48.0)	104 (52.0)	6.98 (4.83–10.1)	5.78 (3.87–8.65)	<0.001	<0.001
Unwitnessed Arrest	23 (8.2)	257 (91.8)	*Ref*			
Witnessed Arrest	148 (26.3)	414 (73.7)	3.99 (2.51–6.37)	3.11 (1.86–5.21)	<0.001	<0.001
No Bystander CPR	109 (18.1)	492 (81.9)	*Ref*			
Bystander-Performed CPR	62 (25.7)	179 (74.3)	1.56 (1.10–2.23)	–	0.01	–
No Bystander AED	153 (18.9)	657 (81.1)	*Ref*			
AED prior to First Responder Arrival	18 (56.3)	114 (43.7)	5.52 (2.69–11.3)	–	<0.001	–
Arrest only prior to First Responder Arrival	138 (18.5)	608 (81.5)	*Ref*			
Arrest after First Responder Arrival	33 (34.4)	63 (65.6)	2.31 (1.46–3.66)	–	<0.001	–
No Mechanical CPR	52 (36.6)	90 (63.4)	*Ref*			
Use of Mechanical CPR	119 (17.0)	581 (83.0)	0.35 (0.24–0.53)	0.53 (0.33–0.86)	<0.001	0.01
No Vasopressors	166 (21.3)	615 (78.7)	*Ref*			
Dopamine or Push Dose Epi			0.33 (0.13–0.84)	–	0.02	–
Non-Invasive, Other Airway	63 (47.4)	70 (52.6)	*Ref*			
Supraglottic Airway	52 (17.4)	246 (82.6)	0.24 (0.15–0.37)	0.35 (0.20–0.59)	0.002	0.08
Endotracheal Tube	56 (13.6)	355 (86.4)	0.18 (0.11–0.27)	0.26 (0.14–0.43)	<0.001	<0.001
			Goodness of Fit	Chisq = 12.2	df = 8	$p = 0.14$

not hypotensive had a good neurologic outcome compared to 11 (10.3%) of 107 hypotensive patients who had a good neurologic outcome. 5 of those 11 hypotensive patients received vasopressors, all of which were dopamine. Hypotensive patients who were treated with dopamine or push-dose epinephrine versus those who were hypotensive and not treated with vasopressors had no significant difference in neurologic outcome (odds ratio of 0.30 versus 0.38, respectively) See Table 1.

4. Discussion

Our research correlates with previous studies suggesting hypotension is associated with a worse neurologic outcome after OHCA. Among those ROSC patients with hypotension, 57% of them received treatment with vasopressors and our data suggest these medications do not improve neurologic outcomes significantly.

What remains unclear is whether fixing that hypotension, especially in the prehospital setting, would affect outcome. While we had some data that vasopressor use had similar outcomes to those who were hypotensive and did not receive vasopressors, we had a small sample of 61 patients. We did not have access to data detailing fluid administration, which is the first-line treatment for post-ROSC hypotension in Alameda County. We also did not have dynamic blood pressure data of the patients progress throughout the EMS encounter, but rather we just had the first and last blood pressure. Additionally, the first blood pressure was typically not a useful data point because it was often recorded as "0" instead of being the first blood pressure after ROSC. Treating a heterogenous pool of patients with a variety of presentations the same by using their final blood pressure is likely causing us to miss out on many subtleties of resuscitation and how ROSC is achieved and sustained, and how blood pressure reacts to vasopressor administration.

We only analyzed key portions of the prehospital patient care record and the corresponding CARES data and were not able to delve into other important variables that may have affected patient outcome. Compression fraction, depth, duration of the arrest, and other data that is typically stored on the cardiac monitor and not recorded directly into the patient care record were not readily accessible on retrospective analysis. These data could have affected outcome, especially given the relatively small sample size.

Despite being in our prehospital protocols for patients with SBP < 90 mmHg after ROSC, only 49 patients received dopamine, and 12 received push-dose epinephrine during our study period. We did not formally analyze the push-dose epinephrine and dopamine subgroups separately given the small sample size. Survival was slightly higher among those who received dopamine (10/48 compared to 2/13 in the push dose epinephrine group) and there were 0 with a good neurologic outcome, compared to 1 with dopamine. The survivor who received dopamine also had a witnessed arrest with bystander CPR and a shockable initial rhythm, so the vasopressor was likely not the major contributing factor to positive outcome.

Other vital signs, such as end-tidal CO_2, may have also contributed to our understanding of patient outcome and prognosis. While initial and final $EtCO_2$ data was collected, a large proportion were recorded as "null" and we therefore did not proceed with analysis. $EtCO_2$ could have been a helpful predictor in survival, since increased acidosis is associated with worse outcome [18].

46 patients in our study had a final recorded blood pressure reading of <90 mmHg and did not receive vasopressors. This could be a missed opportunity to use a potentially helpful medication to increase cerebral perfusion in a patient experiencing hypotension after ROSC. It could also reflect several other factors, such as being right outside the ED doors and providers elected to not delay transfer to administer medication. Additionally, our protocol in Supplement 1 directs the paramedic to provide to give a 500 cc fluid challenge before moving to vasopressors, which means by the time the crew has reached that point in the protocol, they may already be arriving at the ED. The crew also must balance other priorities, including obtaining an EKG, packaging the patient, calling the hospital, etc. There may also be a culture and general pressure to get the patient to the ED as quickly as possible as opposed to "staying and playing" with the patient on scene and stabilizing them.

Despite an association between post-ROSC hypotension and poor neurologic outcome both in our study and previous studies, it still is not known if hypotension causes a poor outcome, or if hypotension is just a feature of someone who would have had a poor outcome anyway. Patients with poor outcomes are more likely to have reperfusion injury, neurologic and cardiovascular damage, which would contribute to hypotension.

5. Conclusion

Prehospital, post-ROSC vasopressors care is complex and aimed at maximizing survival and neurologic outcome by minimizing hypotension and addressing reversable causes of the arrest. Minimizing cerebral hypotension and hypoxia can minimize the devastating neurologic sequalae of survivors, but how and when to treat hypotension remains unclear. Our study was able to compare prehospital hypotension and compared to neurologic outcome, but the utility and efficacy of prehospital treatment of hypotension with vasopressors remains unclear.

Future studies should further examine hypotensive patients who did and did not receive prehospital vasopressors to determine whether or not addressing hypotension with vasopressors affects neurologic outcome.

Disclosures

No disclosures.

Funding

None.

Declaration of Competing Interest

None.

Acknowledgements

Thank you to Newton Addo, who helped with statistical analysis of our data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2021.05.073.

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