Received: 16 October 2020 | Revised: 24 June 2022 | Accepted: 6 July 2021

DOI: 10.1002/emp2.12521

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
Open Access

WILEY

ORIGINAL RESEARCH

Emergency Medical Services

Administration of epinephrine by advanced emergency medical technicians for out-of-hospital cardiac arrest in a rural emergency medical services system

Jared J. Bomba MD[1] | Jamie Benson BA, AEMT[2] | David Hosmer PhD[3] | Daniel Wolfson MD[4,5]

[1] Department of Surgery, Larner College of Medicine at the University of Vermont, Burlington, Vermont, USA

[2] Department of Radiology, Larner College of Medicine at the University of Vermont, Burlington, Vermont, USA

[3] Department of Mathematics and Statistics, University of Vermont, Burlington, Vermont, USA

[4] Department of Surgery, Division of Emergency Medicine, Larner College of Medicine at the University of Vermont, Burlington, Vermont, USA

[5] Vermont Department of Health Division of Emergency Preparedness, Response & Injury Prevention, Burlington, Vermont, USA

Correspondence
Jared James Bomba, MD, Department of Surgery, Larner College of Medicine at the University of Vermont, 89 Beaumont Avenue, Burlington, VT 05405, USA.
Email: jared.bomba@med.uvm.edu

Funding and support:
By *JACEP Open* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

Objective: Epinephrine in out-of-hospital cardiac arrest (OHCA) remains controversial and understudied in rural emergency medical services (EMS) systems. We evaluated the effects of allowing advanced emergency medical technicians (AEMTs) to administer epinephrine during OHCA in a rural EMS system.

Methods: An interrupted time series study was conducted using statewide EMS electronic records. Patients with OHCA before (phase I) and after (phase II) a protocol change expanding the AEMT scope of practice to include epinephrine for OHCA were identified. Number and timing of initial epinephrine administration, return of spontaneous circulation, and 30-day survival rates were compared using descriptive statistics, logistic regression, regression discontinuity, and propensity score matching.

Results: A total of 1037 OHCAs met the inclusion criteria. In phase 1 compared with phase 2, 275 (56.12%) patients received epinephrine versus 624 (83.53%; $P < 0.001$). The mean time to first administration of epinephrine for unwitnessed and bystander-witnessed OHCA were 11.73 minutes versus 8.17 minutes ($P < 0.001$) and 11.59 minutes versus 8.85 minutes ($P < 0.01$), respectively. Unadjusted analysis showed a decrease in 30-day survival rates among patients receiving epinephrine from 18.01% to 12.66% ($P < 0.05$). Adjusted analysis showed an increase in 30-day survival with decreased time to first epinephrine dose(OR 0.960, 1.005; 95% confidence interval, 0.929, 0.992).

Conclusion: Adding epinephrine for OHCA to the AEMT scope of practice was associated with an increased percentage of patients receiving epinephrine and decreased time to first administration of epinephrine for patients with unwitnessed OHCA. Unadjusted analysis showed a decrease in 30-day survival rates among patients receiving epinephrine. Adjusted analysis found that earlier administrationof epinephrine was associated with increased ROSC and 30-day survival.

KEYWORDS
cardiac arrest, EMS, epinephrine, out-of-hospital, pre-hospital, rural

Supervising Editor: Juan March, MD.

1 | INTRODUCTION

1.1 | Background

The American Heart Association estimates 326,000 adult out-of-hospital cardiac arrests (OHCAs) each year are assessed by emergency medical services (EMS) in the United States, of which about 60% are treated.[1] The use of epinephrine in cardiac arrest was proposed as early as 1896[2] for its effects in stimulating cardiac contraction and increasing peripheral vascular resistance, and the practice was adopted during the next century without randomized control trials (RCT). Evidence surrounding the use of epinephrine in unwitnessed OHCA is lacking,[3] yet it remains a mainstay of the advanced cardiac life support (ACLS) algorithm for cardiac arrest.[4]

1.2 | Importance

Previous investigations of OHCA suggest a correlation between epinephrine administration and increased rates of return of spontaneous circulation (ROSC) but with worse neurologic outcomes.[5–7] Meta-analyses support this assessment, finding improved rates of prehospital ROSC[8,9] but no benefit in survival to admission, survival to discharge, or neurologic outcome. The PARAMEDIC2trial further supports these findings with a large RCT showing increased ROSC and worse neurologic outcomes for patients with OHCAreceiving epinephrine.[10] Timing appears important, as early administration of epinephrine has been associated with increased ROSC and improved patient outcomes.[11,12]

Before 2014, in Vermont only paramedics were permitted to administer epinephrine in OHCA or to establishintraosseous access. New EMS protocols for advanced emergency medical technicians (AEMTs) introduced in 2014 added the option of obtaining intraosseous versus intravenous access and administration of cardiac-dosing epinephrine during OHCA. In Vermont's rural EMS system, many EMS agencies use AEMTs rather than paramedics as the highest level practitioner on the ambulance crew. AEMTs are more widely dispersed throughout the state and often arrive well in advance of a paramedic at many OHCAs. Concern that a delay in epinephrine administration might adversely affect rates of ROSC influenced the decision to include epinephrine in the AEMT protocol.

1.3 | Goals of investigation

It was hypothesized that allowing AEMT administration of epinephrine in OHCA would increase the number of patients receiving epinephrine, shorten the average time to first epinephrine administration, and improve rates of ROSC and patient outcomes.

The Bottom Line

Although use of epinephrine by advanced emergency medical technicians in out-of-hospital cardiac arrest (OHCA) showed an overall increase in 30-day mortality, earlier administration of epinephrine was associated with a decrease in 30-day mortality. This study supports prior research that has shown a benefit for early epinephrine administration in OHCA.

2 | METHODS

2.1 | Study design and setting

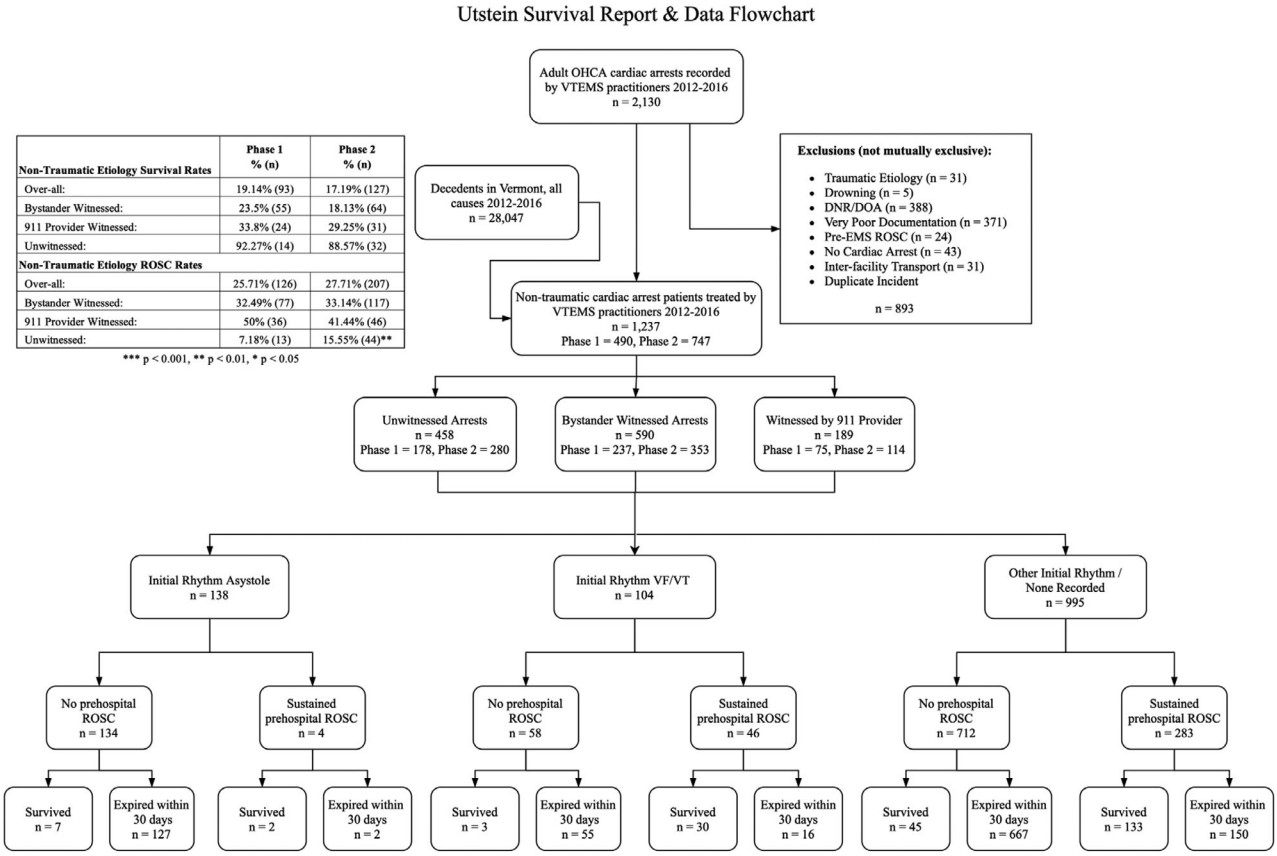
We used an interrupted time series study design to describe the effects of expanding the AEMT scope of practice in Vermont EMS to include epinephrine during OHCA. Vermont is a small rural state with a population of ≈625,000 people distributed across 9216 miles, averaging 68 persons per square mile.[13] This study was approved by the University of Vermont Institutional Review Board.

2.2 | Epinephrine in cardiac arrest protocol change

In phase1 of this study, January 1, 2012, through December 31, 2013, protocol allowed only paramedics to administer epinephrine during OHCA, whereas other EMS practitioners focused on high-quality cardiopulmonary resuscitation (CPR) and automated external defibrillator (AED) use. In phase 2 of this study, April 1, 2014, through March 31, 2016, new Vermont statewide EMS protocols were instituted allowing AEMTs to administer 1-mg epinephrine (1:10,000) intravenously or intraosseously every 3 to 5 minutes during OHCA. A training and adoption period from January 1, 2014, to March 31, 2014, was excluded. In addition, the updated EMS protocols added intraosseous access to the AEMT scope of practice and a termination of resuscitation (TOR) protocol for all practitioner levels.

2.3 | Emergency medical services

During the study period, there were 89 transporting and 94 nontransporting EMS agencies in Vermont. These were staffed by ≈3095 EMS personnel in phase 1, including 1001 intermediate levels (AEMT and emergency medical technician–intermediate) and 86 paramedics, and 3611 EMS personnel in phase 2, including 860 AEMTs and 333 paramedics (R. Walker, personal communication, 2020). The remaining personnel were certified at the basic life support level.



Non-Traumatic Etiology Survival Rates	Phase 1 % (n)	Phase 2 % (n)
Over-all:	19.14% (93)	17.19% (127)
Bystander Witnessed:	23.5% (55)	18.13% (64)
911 Provider Witnessed:	33.8% (24)	29.25% (31)
Unwitnessed:	92.27% (14)	88.57% (32)
Non-Traumatic Etiology ROSC Rates		
Over-all:	25.71% (126)	27.71% (207)
Bystander Witnessed:	32.49% (77)	33.14% (117)
911 Provider Witnessed:	50% (36)	41.44% (46)
Unwitnessed:	7.18% (13)	15.55% (44)**

*** p < 0.001, ** p < 0.01, * p < 0.05

FIGURE 1 Unadjusted outcomesand Utstein survival report for out-of-hospital cardiac arrests recorded by Vermont EMS practitioners from January 1, 2012, to December 31, 2016. Base mortality and return of spontaneous circulation rates by study phase are found in the embedded table. DNR, do not resuscitate; DOA, dead on arrival; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation; VTEMS, Vermont EMS; VF, ventricular fibrillation; VT, ventricular tachycardia

2.4 | Study population

The study population consisted of all adult patients with OHCA identified in phase 1 and phase 2. Cases were included only if cardiac arrest occurred outside of a hospital, the patient was aged >18 years at the time of the incident, no trauma immediately preceded the event (including strangulation and drowning), and the patient received CPR from EMS. Cases were also excluded if there were significant documentation errors. See Figure 1 for a full breakdown of included and excluded subjects and Utstein outcomes.

2.5 | Data collection

Prehospital data were obtained from the Vermont Statewide Incident Reporting Network (SIREN; ImageTrend, Lakeville, MN), an electronic reporting system used by all Vermont EMS agencies. Cases were included that had a primary impression of "cardiac arrest" or the primary symptoms "cardiorespiratory arrest" or "death" or cases where cardiac arrest–specific fields were completed in the incident report. All cases were examined via narrative review to confirm accuracy of information.

Mortality data were obtained from the Vermont Department of Health, Vital Records, including identifiers and date, manner, and underlying causes of death. Decedents were probabilistically matched to SIREN records using Match*Pro 1.6.2 (National Institutes of Health Division of Cancer Control & Population Sciences, Bethesda, MD). Blocking variables used included patient name and date of birth. Names were matched using the Soundex phonetic system, and birth dates were matched using Levenshtein distance. The default m-probabilities and match thresholds were used, with a 95% match confidence cut-off for selection. Match*Pro was also used in "deduplication" mode to match paramedic intercepts with primary 9-1-1 calls and ensure that cases appeared only once in the data set. These matched intercepts were manually reviewed to ensure accuracy.

2.6 | Outcome measures

The primary outcome measures were (1) percentage of patients receiving epinephrine and (2) time to first administration of epinephrine. The secondary outcome measures were (1) ROSC and (2) 30-day survival.

ROSC, 30-day survival, and time to first epinephrine administration were compared for witnessed and unwitnessed OHCAs in phase 1 and

phase 2. ROSC was identified by search criteria in the SIREN prehospital care report and narrative review after an OHCA in the same prehospital care report. Witnessed arrests were those observed by either an EMS practitioner or a bystander and are separated as indicated. ROSC was considered sustained after either 15 minutes or if present on destination arrival, whichever occurred first.

Time to first administration of epinephrine was defined as the time from the initial advanced life support (ALS) arrival (AEMT, emergency medical technician–intermediate, or paramedic) to first dose for unwitnessed or bystander-witnessed OHCA. Time to first administration of epinephrine for EMS practitioner–witnessed OHCA was defined as the time from initiation of CPR to first dose.

2.7 | Statistical analysis

Comparisons between phase 1 and phase 2 were made using a 2-sample *t* test, chi-squared test, or Kruskal-Wallis H test as appropriate. Statistical significance was defined as a 2-sided *P* value ≤0.05. To estimate the effect of the protocol change on 30-day survival and ROSC, we built 2 logistic regression models. Variables were considered for model inclusion based on clinical relevance, literature review, and statistical significance in univariate and fractional polynomial analyses. ROSC and 30-day survival were binary response variables and assumed to be independent. Results from these 2 models are reported as odds ratio (OR) with 95% confidence intervals (CIs). To better visualize the effect of the protocol change on time to epinephrine administration, we employed a regression-discontinuity analysis using the rdrobust package in Stata/SE 16.1 (StataCorp LLC, College Station, TX). Propensity score matching was used to estimate the average treatment effect of the protocol expansion on epinephrine administration timing. Analysis was conducted using the psmatch2 package with single nearest-neighbor matching on patient sex, age, witnessed arrest status, pre-EMS defibrillation status, response interval, on-scene interval, route of administration, and administering practitioner level. As the propensity score match is built on the logistic regression model, the model's Akaike information criterion, Bayesian information criterion, and Hosmer-Lemeshow test were used to assess fit.

3 | RESULTS

3.1 | Patient demographics

In phase 1, there were 490 OHCAs treated by EMS with 75 (15.31%) witnessed by EMS practitioners, 237 (48.37%) bystander witnessed, and 178 (38.57%) unwitnessed. In phase 2, there were 747 OHCAs treated by EMS with 114 (15.26%) witnessed by EMS practitioners, 353 (47.26%) bystander witnessed, and 280 (37.48%) unwitnessed. The median on-scene interval in phase 1 was 17.48 minutes and 24.03 minutes in phase 2 ($P < 0.001$), and the median response interval in phase 1 was 6.55 minutes and 8.74 minutes in phase 2 ($P < 0.05$). See Table 1 and Figure 1.

TABLE 1 Characteristics of patients with out-of-hospital cardiac arrest treated by Vermont emergency medical services

Variable	Phase 1, n = 490	Phase 2, n = 747
Demographics		
Female sex, n (%)	152 (31.02)	248 (33.20)
Age, mean in years	64.58	63.69
Time, median in minutes		
Response interval	6.55	8.74*
On-scene interval	17.48	24.03***
Transport interval	10.92	10.92
Location, n (%)		
Home/residence	355 (72.45)	522 (69.88)
Healthcare facility	33 (6.73)	62 (8.30)
Trade or Service	26 (5.31)	39 (5.22)
Street or highway	28 (5.71)	41 (5.49)
Public building	13 (2.65)	17 (2.28)
Place of recreation of sport	11 (2.24)	13 (1.74)
Other location	24 (4.9)	53 (7.1)

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

3.2 | Primary outcome measures

In phase 1, 275 (56.12%) patients received epinephrine, whereas in phase 2, 624 (83.53%) patients received epinephrine ($P < 0.001$). In phase 1, all patients who received epinephrine were given the first dose by a paramedic, whereas in phase 2, 212 (36.55%) patients were given their first dose by an AEMT ($P < 0.001$). There was also a significant increase in the number of first doses that were administered by the intraosseous route (primarily anterior tibial) with 125 (45.79%) in phase 1 and 431 (69.74%) in phase 2 ($P < 0.001$). The mean time to first administration of epinephrine for unwitnessed OHCA was 11.73 minutes in phase 1 and 8.17 minutes in phase 2 ($P < 0.001$). The mean time to first administration of epinephrine for bystander-witnessed OHCA was 11.59 minutes in phase 1 and 8.85 minutes in phase 2 ($P < 0.001$). Paramedics had a higher mean first dose administration time in phase 1 (11.24 minutes) compared with phase 2 (8.02 minutes), whereas the mean AEMT first dose administration time in phase 2 was 9.33 minutes. See Table 2.

Bias-corrected regression discontinuity revealed no significant difference in average treatment effect in time to first dose of epinephrine between phase 1 and phase 2 (−3.97 minutes; 95% CI, −12.355 to 4.414). See Figure 2. However, propensity score matching revealed an estimated treatment effect in time to first dose of epinephrine between phase 1 and phase 2 of −4.32 minutes (95% CI, −5.993 to −2.655).

3.3 | Secondary outcome measures

In our unadjusted analysis, between phase 1 and phase 2, there was no significant change in ROSC rate (23.27% vs 23.08%; $P > 0.05$),

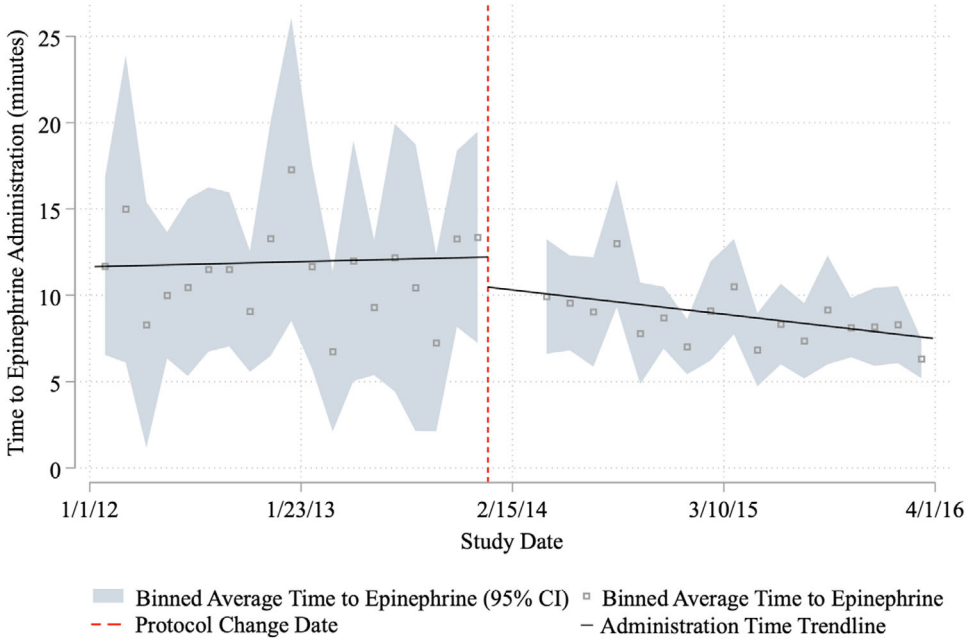


FIGURE 2 Regression discontinuity plot showing the change in epinephrine administration rate throughout the study. Administration times are binned by date, and a first-order polynomial is fit to represent the average within the bin (represented by gray points). The 95% confidence interval (CI) for administration time across bins is shaded in blue, and the trendline for administration time within each phase in black. The difference in administration time after study phase change (dotted red line) constitutes the estimated treatment effect between phases

but there was a decrease in 30-day survival from 18.01% to 12.66% ($P < 0.05$) for patients who received epinephrine. In our adjusted analysis, between phase 1 and phase 2, ROSC did not have a statistically significant correlation with study group (OR, 1.104; 95% CI, 0.747–1.739) but did correlate with time to first epinephrine dose (OR, 0.974; 95% CI, 0.950–0.999). In addition, 30-day survival was not associated with study group (OR 0.759; 95% CI, 0.466–1.236), but was associated with increased time to first epinephrine dose (OR 0.960; 95% CI, 0.929, 0.992). See Table 3.

3.4 | Limitations

One limitation of this study is the number of EMS agencies recording data in SIREN during phase 1 and phase 2. As SIREN was being introduced statewide during phase 1, some EMS agencies had not yet started reporting into this system so that data from OHCAs to which those agencies responded were unavailable. Because our models were limited in power, there would be benefit from a larger randomized controlled trial regarding the efficacy of epinephrine in OHCA in rural EMS systems. We recognize that with generally low OHCA survival and a limited study population due to this study being set in a small, rural area, our ability to assess the significance of findings is limited. In addition, a significant amount of data were unusable due to poor or missing documentation. Finally, another limitation was a lack of neurologic outcomes data, as we did not have the ability to link to hospital records. We recognize that neurologic outcomes would have provided additional information about the status of OHCA survivors; however, given these limitations, we used ROSC and 30-day survival. We recognize that this is an imperfect marker; however, we believe that the first step in any improvement in outcomes is survival.

Because of the limited documentation, we were unable to reliably assess which sites were used for intraosseous placement during the study; however, based on known practices, we believe the proximal tibia was the primary intraosseous site used. This is strongly suspected to be associated with a decrease in medication effectiveness. We suspect epinephrine administration via the anterior tibial intraosseous site may have nullified some of the potential positive effect of epinephrine for the patients in this study.

4 | DISCUSSION

We evaluated the effect of introducing epinephrine during OHCA to the AEMT scope of practice. We found a significant increase in the percentage of patients receiving epinephrine and a decrease in time to first dose administration between phase 1 and phase 2. The increase in overall number of patients receiving epinephrine and the reduction in time to first dose seems reasonable considering the significant number of EMS practitioners enabled to administer this medication and the time practitioners had to gain experience administering the medication throughout the study period. In phase 1, several patients who received epinephrine only did so after a paramedic intercepted a non-paramedic transporting agency, resulting in longer times between initiation of care by ALS practitioners and first administration of epinephrine. Allowing AEMTs to administer epinephrine without the need to wait

TABLE 2 Timing, frequency, and route of epinephrine administration by Vermont emergency medical services advanced life support practitioners by study period and licensure level

Variable	Phase 1	Phase 2
All patients, % (n)		
30-Day Survival	19.14% (93)	17.19% (127)
Prehospital return of spontaneous circulation	25.71% (126)	27.71% (207)
Patients receiving epinephrine, % (n)	56.12% (275)	83.53% (624)***
First dose by AEMT practitioner	–	36.55% (212)
First dose by intraosseous route	45.79% (125)	69.74% (431)***
30-Day Survival	18.01% (49)	12.66% (78)*
Prehospital return of spontaneous circulation	23.27% (64)	23.08% (144)
Time to first epinephrine, mean in minutes	11.24	8.58***
EMS witnessed arrest	9.2	8.81
Bystander witnessed	11.59	8.85**
Unwitnessed arrest	11.73	8.17***
Paramedic administered	11.24	8.02***
AEMT administered	–	9.33

AEMT, advanced emergency medical technician; EMS, emergency medical services.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

TABLE 3 Logistic regression models predicting 30-day survival and return of spontaneous circulation for out-of-hospital cardiac arrest patients treated by Vermont EMS

Variable	30-Day Survival Model Odds Ratio (95% CI)	ROSC Model Odds Ratio (95% CI)
Pre/Post Epi Group	0.759	1.140
	(0.466; 1.236)	(0.747; 1.739)
Time to Epinephrine	0.960*	0.974*
	(0.929; 0.992)	(0.950; 0.999)
Bystander Defibrillation	1.923*	1.637*
	(1.165; 3.176)	(1.054; 2.542)
Patient Age	0.979***	0.996
	(0.967; 0.991)	(0.986; 1.007)
Patient Sex - Male	0.610*	0.553**
	(0.394; 0.942)	(0.386; 0.795)
On-Scene Interval	0.983*	0.992
	(0.968; 0.998)	(0.982; 1.002)
Response Interval	0.978	0.951***
	(0.945; 1.012)	(0.923; 0.980)
Witnessed Status	1.755*	2.897***
	(1.110; 2.773)	(1.955; 4.291)
First Dose by Paramedic	1.822	1.271
	(0.998; 3.326)	(0.811; 1.992)
First Dose Intravenous Route	1.027	1.135
	(0.657; 1.605)	(0.786; 1.640)

*** p<0.001, ** p<0.01, * p<0.05

for a paramedic likely reduced the time to initial epinephrine administration for patients who would have received epinephrine in either period; however, it is worth noting that the mean time for paramedics to administer epinephrine also decreased from phase 1 to phase 2, which may indicate overall systems-level improvement in getting resources to patients more rapidly. In addition, regression discontinuity shows a downward trend in time to first epinephrine dose during phase 2 (when AEMTs were added); these findings combined suggest system-level improvements in administration timing and prevalence. Furthermore, the propensity score matching suggests that allowing AEMTs to administer epinephrine was likely a significant factor for the reduction in time to first dose between study phases.

Not all cases where epinephrine was not given were attributed to an inability of personnel to administer it. Commonly cited reasons for epinephrine not being administered included rapid ROSC after initial defibrillation, other immediate interventions for reversible causes, inability to obtain intravenous or intraosseous access, lack of sufficient staffing, and proximity to destination at time of arrest. Therefore, we would not expect epinephrine to be administered to 100% of patients even under ideal circumstances.

Our unadjusted analysis found no change in ROSC across study phases but a significant decrease in 30-day survival between phase 1 and phase 2 for patients who received epinephrine. Our logistic regression analysis found that significant predictors of ROSC were response interval, bystander-witnessed OHCA, bystander defibrillation, patient sex. We also found that significant predictors of 30-day survival were patient age, patient sex, bystander defibrillation, bystander-witnessed OHCA, and time to epinephrine administration. Notably, study phase, the EMS practitioner level (paramedic vs AEMT) administering the first dose of epinephrine, and route of first dose administration were not significant predictors of 30-day survival or ROSC in our adjusted model. The finding of decreased survival in unadjusted analysis raises concern about the role of epinephrine in OHCA in rural EMS systems. Given that this finding was not present on adjusted analysis accounting for all major variables that we were able to assess, it is possible that the finding of decreased survival between study phases was related to a confounding variable rather than the epinephrine itself. It is, however, also possible that epinephrine itself is responsible for this decrease in survival. The finding that earlier epinephrine administration was associated with increased 30-day survival suggests the possibility that epinephrine may be beneficial in early OHCA yet harmful later in OHCA. That finding, however, may be biased by the earliest epinephrine doses being administered in patients with EMS-witnessed OHCA and therefore may be confounded by it. We strongly recommend further investigation of the potential for epinephrine administration during OHCA to decrease survival, specifically in rural EMS systems. The findings of association between response interval, bystander intervention, and age are logical findings that serve as a check on the

model itself as we know that typically patients who are younger, who received earlier intervention, and who are reached more rapidly by EMS will likely have better outcomes than older patients or those who have a longer downtime before treatment.

Our findings are consistent with 2 prior studies that showed improved outcomes when epinephrine was administered within 20 minutes yet poorer outcomes if delayed longer[14,15] as well as a study that found each minute of delay impacts survival and functional outcomes.[16] A small RCT from 2011[17] and a larger, novel post hoc analysis of an RCT of overall ACLS interventions[18] an increase in ROSC related to epinephrine. Based on this evidence, further research in rural settings is required to determine whether there is tangible benefit to adding this intervention to the scope of intermediate level EMS practitioners. Furthermore, better powered studies should investigate how to improve outcomes for survivors of cardiac arrest and further assess the relationship between early epinephrine administration and sustained ROSC.

Some potentially confounding factors have been investigated previously. The TOR protocol was introduced at the same time in the same EMS system. A prior study by Jordan et al demonstrated the effectiveness in implementing the TOR protocol in Vermont using the same periods of time as in our study in a smaller region of the state.[19] Intraosseous access for AEMTs was also introduced at the same time, and the addition of intraosseous access has been shown to reduce time to administration of medications, to be equally effective for AEMTs and paramedics,[20] and to have no significant association with the effectiveness of those medications.[21,22] However, evidence does exist to suggest that the intraosseous site selection between the proximal humeral and anterior tibial may play a significant role in medication effectiveness[23] and that sternal intraosseous placement warrants consideration as a potentially superior option,[24] although this site may be impractical with ongoing CPR. We recommend further investigation of intraosseous versus intravenous access for OHCA in a rural EMS system and further investigation of intraosseous site selection.

The addition of epinephrine for OHCA to the AEMT scope of practice was associated with an increase in the percentage of patients receiving epinephrine and a decrease in the time to first administration of epinephrine for patients with unwitnessed OHCA. Unadjusted analysis showed an increase in 30-day mortality between phases 1 and 2 for patients receiving epinephrine that was not present on logistic regression analysis nor in unadjusted analysis when patients who did not receive epinephrine were included. Earlier administration of epinephrine was associated with a decrease in 30-day mortality. Further investigation of neurologic outcomes with larger study groups is needed to assess whether administration of epinephrine by intermediate-level EMS practitioners offers tangible benefit in OHCA in rural EMS systems. Further investigation is also required to assess the impact of route of administration and intraosseous site selection on medication effectiveness during OHCA.

ACKNOWLEDGMENTS

We acknowledge the hard work and dedication of emergency medical services (EMS) personnel and other first responders across Vermont for their continual commitment to excellence. We also acknowledge Roz Bidad for logistical guidance and Dr. Turner Osler for assistance with statistical analysis and Dr. Stas Amato for general guidance. Finally, we acknowledge Ray Walker, Vermont Department of Health EMS Programs Administrator, for providing data on Vermont EMS services.

AUTHOR CONTRIBUTIONS

Jared J. Bomba contributed to the writing of this text, organization of resources for the project, and development of tables and figures. Jamie Benson contributed to the writing of this text, statistical analysis of data, and development of tables and figures. David Hosmer contributed to the statistical analysis of data and the development of tables and figures. Daniel Wolfson contributed to the editing of this text, inspiration for the project, and overall coordination and guidance.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Jamie Benson BA, AEMT https://orcid.org/0000-0002-0709-4711

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update. *Circulation*. 2015;131(4). https://doi.org/10.1161/cir.0000000000000152
2. Gottlieb R. Ueber die Wirkung der Nebennierenextracte auf Herz und Blutdruck. *Archiv für experimentelle Pathologie und Pharmakologie*. 1896;38(1):99-112.
3. Reardon PM, Magee K. Epinephrine in out-of-hospital cardiac arrest: a critical review. *World J Emerg Med*. 2013;4(2):85-91.
4. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult advanced cardiovascular life support. *Circulation*. 2015;132(18_suppl_2). https://doi.org/10.1161/cir.0000000000000261
5. Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. *JAMA*. 2012;307(11):1161-1168.
6. Loomba RS, Nijhawan K, Aggarwal S, Arora RR. Increased return of spontaneous circulation at the expense of neurologic outcomes: is prehospital epinephrine for out-of-hospital cardiac arrest really worth it?. *J Crit Care*. 2015;30(6):1376-1381.
7. Evans ME, Chassee T. BET 2: usefulness of epinephrine in out-of-hospital cardiac arrest *Emerg Med J*. 2016;33(5):367-368.
8. Lin S, Callaway CW, Shah PS, et al. Adrenaline for out-of-hospital cardiac arrest resuscitation: a systematic review and meta-analysis of randomized controlled trials. *Resuscitation*. 2014;85(6):732-740.
9. Atiksawedparit P, Rattanasiri S, McEvoy M, Graham CA, Sittichanbuncha Y, Thakkinstian A. Effects of prehospital adrenaline administration on out-of-hospital cardiac arrest outcomes: a systematic review and meta-analysis. *Critical Care*. 2014;18(4):463.
10. Perkins GD, Ji C, Deakin CD, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. *N Engl J Med*. 2018;379(8):711-721.
11. Hayashi Y, Iwami T, Kitamura T, et al. Impact of early intravenous epinephrine administration on outcomes following out-of-hospital cardiac arrest. *Circ J*. 2012;76(7):1639-1645.
12. Donnino MW, Salciccioli JD, Howell MD, et al. Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: retrospective analysis of large in-hospital data registry. *BMJ*. 2014;348:g3028.

13. State health assessment 2018. Vermont department of health. https://www.healthvermont.gov/about/reports/state-health-assessment-2018. Published August 7, 2019. Accessed December 1, 2019.
14. Sagisaka R, Tanaka H, Takyu H, Ueta H, Tanaka S. Effects of repeated epinephrine administration and administer timing on witnessed out-of-hospital cardiac arrest patients. *Am J Emerg Med*. 2017;35(10):1462-1468.
15. Ross EM, Mapp J, Kharod C, Wampler DA, Velasquez C, Miramontes DA. Time to epinephrine in out-of-hospital cardiac arrest: a retrospective analysis of intraosseous versus intravenous access. *Am J Disaster Med*. 2016;11(2):119-123.
16. Hansen M, Schmicker RH, Newgard CD, et al. Time to epinephrine administration and survival from nonshockable out-of-hospital cardiac arrest among children and adults. *Circulation*. 2018;137(19):2032-2040.
17. Jacobs IG, Finn JC, Jelinek GA, Oxer HF, Thompson PL. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. *Resuscitation*. 2011;82(9):1138-1143.
18. Olasveengen TM, Wik L, Sunde K, Steen PA. Outcome when adrenaline (epinephrine) was actually given vs. not given—post hoc analysis of a randomized clinical trial. *Resuscitation*. 2012;83(3):327-332.
19. Jordan MR, O'Keefe MF, Weiss D, Cubberley CW, MacLean CD, Wolfson DL. Implementation of the universal BLS termination of resuscitation rule in a rural EMS system. *Resuscitation*. 2017;118:75-81.
20. Wolfson DL, Tandoh MA, Jindal M, Forgione PM, Harder VS. Adult intraosseous access by advanced EMTs: a statewide non-inferiority study. *Prehosp Emerg Care*. 2017;21(1):7-13.
21. Johnson D, Garcia-Blanco J, Burgert J, et al. Effects of humeral intraosseous versus intravenous epinephrine on pharmacokinetics and return of spontaneous circulation in a porcine cardiac arrest model: a randomized control trial. *Ann Med Surg (Lond)*. 2015;4(3):306-310.
22. Wong MR, Reggio MJ, Morocho FR, et al. Effects of intraosseous epinephrine in a cardiac arrest swine model. *J Surg Res*. 2016;201(2):327-333.
23. Feinstein BA, Stubbs BA, Rea T, Kudenchuk PJ. Intraosseous compared to intravenous drug resuscitation in out-of-hospital cardiac arrest. *Resuscitation*. 2017;117:91-96.
24. Pasley J, Miller CHT, DuBose JJ, et al. Intraosseous infusion rates under high pressure: a cadaveric comparison of anatomic sites. *Jl Trauma Acute Care Surge*. 2015;78(2):295-299.

How to cite this article: Bomba JJ, Benson J, Hosmer D, Wolfson D. Administration of epinephrine by advanced emergency medical technicians for out-of-hospital cardiac arrest in a rural emergency medical services system. *JACEP Open*. 2021;2:e12521. https://doi.org/10.1002/emp2.12521