

Patient Outcomes in Relation to the Administration of Epinephrine in Out of Hospital Cardiac Arrests

Paramedic Mini CAT – Fanshawe College

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Clinical Scenario:

You and your partner are dispatched to Exeter, Ontario for a 54-year-old male patient unresponsive. You arrive on scene and confirm that the patient is in cardiac arrest with vital signs absent (VSA). No bystander cardiac pulmonary resuscitation (CPR) was started prior to your arrival. You start a medical cardiac arrest with your partner beginning CPR while you place the pads anterior apex on the patient and analyze the rhythm. The patient has an organized rhythm on the monitor without a palpable pulse meaning he is in pulseless electrical activity. No shock is delivered. Your partner continues CPR while you put in an oral pharyngeal airway (OPA) and start ventilating the patient with the bag valve mask (BVM) hooked up to 15 litres per minute of oxygen. As well, you administer one dose of epinephrine before the second analysis. After two minutes of CPR have passed, you perform another rhythm analysis. The patient is now presenting in coarse ventricular fibrillation, so a shock was delivered to the patient. You take over CPR, while your partner puts in a supraglottic airway (SGA) and you continue to provide CPR and ventilating the patient 10 compressions to one breathe. Your partner prepares the stretcher to ensure you are ready for transport. After two more minutes, the third analysis is completed. The patient is presenting with an organized sinus bradycardia rhythm with a palpable pulse, meaning the patient has experienced a return of spontaneous circulation (ROSC). You perform ROSC care on the patient and initiate transport to the hospital. After successfully transferring care of patient, you are reflecting on the call and wonder what the rate of survival is and overall patient outcome among those who receive epinephrine during an out of hospital cardiac arrest (OHCA).

Background

The usage of epinephrine in cardiac arrests has been supported and used in the clinical field of paramedicine for around 50 years. Much of the research surrounding use of epinephrine have been supporting the usage of such intervention by showing that patients who received epinephrine during an OHCA had an increased likelihood of ROSC and overall survival rate to discharge from hospital. The mechanism of action of epinephrine is that it stimulates alpha receptors in vascular smooth muscle, which causes vasoconstriction. In sequence, there is an increase in aortic diastolic pressure, which leads to increased coronary perfusion pressure which is linked to an increased chance of ROSC. The usage of epinephrine during OHCA results in an increase in myocardial blood flow. However, emerging research has linked epinephrine to reductions in microvascular blood during resuscitation and after. Thus, showing that epinephrine impairs cerebral blood flow leading to worsened neurological outcomes proceeding OHCA. Therefore, epinephrine may result in improved ROSC likelihood among OHCA, but does it worsen the patients overall neurological status.

The literature explores epinephrine vs. placebo effects on ROSC, whether the timing of epinephrine administration upon arrival to OHCA influences patient outcome, the effects epinephrine has on cerebrovascular blood flow, whether epinephrine administration and the patients ECG rhythm presenting in a shockable or non-shockable rhythm influences overall outcome and patients' neurological outcomes proceeding epinephrine intervention during OHCA.

Review question

Patient/Problem – Patients suffering from cardiac arrest in the prehospital setting

Intervention – effectiveness of epinephrine

Comparison/control – versus no epinephrine usage

Outcome – looking at patient outcome and percentage of ROSC achieved

In the prehospital setting does the usage of epinephrine versus no epinephrine result in an increased survival rate, better patient outcomes and a higher chance of getting a ROSC among OHCA patients.

Search strategy (Basic): prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service AND epinephrine or adrenaline AND cardiac arrest or heart arrest or cardiopulmonary arrest.

Limits: Full text, 2016-2022, academic journals

Databases searched: Medline and CINHALL

Search results: Medline (38) and CINHALL (14)

Included for review: 5 studies were reviewed. They were reviewed because they had been published in the past recent years: 2016 to 2022. They were also chosen as they looked at effects of epinephrine in improving the likelihood of getting a ROSC as well as overall better patient outcome after resuscitation, such as favorable neurological outcomes.

Title, author, year	Study design, Question/Purpose, LOE	Population	Outcomes	Results	Weaknesses & Strengths
<p>Title:</p> <p>Association of Timing of Epinephrine Administration with Outcomes in Adults with Out-of-Hospital Cardiac Arrest</p> <p>Authors:</p> <p>Masashi Okubo, Sho Komukai, Clifton Callaway and Junichi Izawa</p> <p>Year Published:</p> <p>2021</p>	<p>Study Design:</p> <p>The study design was observational cohort study.</p> <p>It was a secondary analysis that included data from OHCA patients in the resuscitation outcomes consortium (ROC) network.</p> <p>ROC conducted a study trial involving OHCA patients treated by EMS at 10 sites across North America from April 1, 2011, till June 30, 2015.</p> <p>Researchers obtained data from the ROC network of OHCA and performed a secondary data analysis from May 2019 till April 2021.</p>	<p>Inclusion Criteria:</p> <p>The population consisted of adults 18 years old or older with EMS-treated, non-traumatic OHCA by EMS.</p> <p>Exclusion Criteria:</p> <p>The exclusion criteria consisted of EMS-witnessed OHCA, those without advanced life support involvement, those in whom resuscitations were terminated in the prehospital setting because of DNR, those with missing data on age, initial cardiac rhythm, epinephrine</p>	<p>Variable Measured:</p> <p>Age, sex, race, cause of OHCA, initial rhythm, location of cardiac arrest, whether arrest was witnessed, layperson CPR, shock delivered prior to arrival, advanced airway management, departure from scene.</p> <p>Primary:</p> <p>The primary outcome in the study was survival to hospital discharge.</p> <p>Secondary:</p> <p>The secondary outcome included</p>	<p>The median intervals between EMS arrival and epinephrine administration were 7.3 minutes in those with shockable rhythms and 8.1 minutes in those with no shockable rhythms.</p> <p>For shockable rhythms, receipt of epinephrine was not associated with survival to hospital discharge compared to being at risk of receiving epinephrine.</p> <p>Epinephrine was not linked to survival at discharge but was linked to prehospital ROSC.</p>	<p>Strengths:</p> <p>Large sample size (n=41079).</p> <p>Used time dependent propensity score-matched cohort after original cohort.</p> <p>Included resuscitation time bias and time-varying confounders.</p> <p>Weaknesses:</p> <p>Sex distribution not similar: male dominant.</p> <p>Only age (18+).</p> <p>Large differential sample sizes between epinephrine and no epinephrine administration in both shockable and non-</p>

Title, author, year	Study design, Question/Purpose, LOE	Population	Outcomes	Results	Weaknesses & Strengths
	<p>Question/Purpose:</p> <p>Is timing of epinephrine administration associated with outcomes in adults with out-of-hospital cardiac arrests?</p> <p>LOE – IV</p>	<p>administration status, and primary outcome, those who received vasopressin or endotracheal epinephrine administration; and those with missing or negative values in resuscitation time variables.</p> <p>Total Population:</p> <p>Total study population was n=<u>41 079</u> patients.</p> <p>Split further into shockable cardiac rhythms: epinephrine administered (n=8223) and no epinephrine (n=1865) and non shockable cardiac rhythms: epinephrine</p>	<p>favorable functional status at hospital discharge, which was defined as a modified Rankin Scale of 3 or lower and prehospital ROSC.</p>		<p>shockable rhythm groups.</p> <p>Only medical cardiac arrests.</p> <p>Limitations:</p> <p>Timing of epinephrine administration may be due to EMS skills.</p> <p>Unable to adjust for unmeasured confounders.</p> <p>Unable to assess a causation due to observational study design.</p> <p>May not be generalizable to other EMS systems.</p>

Title, author, year	Study design, Question/Purpose, LOE	Population	Outcomes	Results	Weaknesses & Strengths
		administered (n=27901) and no epinephrine (n=3090).			

Title:	Study Design:	Inclusion Criteria:	Measured Variable:	Results:	Strengths:
<p>Effectiveness of Prehospital Epinephrine Administration in Improving Long-term Outcomes of Witnessed Out-of-hospital Cardiac Arrest Patients with Initial Non-shockable rhythms</p> <p>Authors:</p> <p>Jun Tomio, Shinji Nakahara, Hideto Takahashi, Masao Ichikawa, Masamichi Nishida, Naoto Morimura and Tetsuya Sakamoto</p> <p>Year Published:</p>	<p>Controlled, propensity-matched, retrospective cohort study using Japan's nationally representative data from nationwide registry of OHCA patients between January 2008 to December 2012.</p> <p>Question/Purpose:</p> <p>The study looked to examine the effects of prehospital epinephrine administration in OHCA patients with non-shockable rhythms, PEA, and asystole.</p> <p>LOE – IV</p>	<p>OHCA patients aged 15-94 years old with initial recorded non-shockable rhythm (pulseless electrical activity and asystole) that were witnessed by a bystander.</p> <p>Exclusion Criteria:</p> <p>Exclusion criteria was cardiac arrests that occurred after arrival of EMS, ROSC before arrival of EMS, epinephrine use after ROSC because of re-arrest, arrests attributable to external causes.</p> <p>Patients with missing, contradictory, or</p>	<p>Year OHCA occurred, season, sex, age, bystander CPR, AED by bystander, EMS call to contact time, cardiac origin, family member present, airway management, attempted defibrillation, EMS to hospital arrival interval and patient outcome.</p> <p>Primary:</p> <p>The primary outcome was neurologically intact survival, which was defined as CPC score of 1-2 at 1 month or at discharge, whichever was earlier.</p> <p>Secondary:</p> <p>The secondary outcome was survival at 1 month or at discharge.</p>	<p>PEA survival was 2499 (5.6%)</p> <p>PEA neurologically intact was 943 (2.1%)</p> <p>Asystole survival was 1185 (1.8%)</p> <p>Asystole neurologically intact was 281 (0.4%)</p> <p>Over the study period the amount of epinephrine administration increased yearly regardless of the initial rhythm.</p> <p>Epinephrine administered PEA patients were more likely to survive than control patients, but there was no significant difference in</p>	<p>Clear focused question they looked to answer with sufficient rationale.</p> <p>Lengthy review period (4 years)</p> <p>Large sample size (n=110239)</p> <p>Used 1-1 matched pairs of patients with or without epinephrine.</p> <p>Weaknesses:</p> <p>Only ages (15+).</p> <p>Differences in sample sizes for PEA and asystole and epinephrine vs. no epinephrine.</p> <p>Only witnessed arrests by bystanders.</p> <p>Limitations:</p>

2017		<p>outlying time data, those with missing data for calculation of propensity scores and those with missing data for outcome variables and/or epinephrine administration were excluded.</p> <p>Total Population:</p> <p>Total eligible for inclusion was n=574 840. After exclusion criteria, the total population in the study was <u>n=110239</u>.</p> <p>Further division into PEA: epinephrine administered (n=9226) or no epinephrine (n=35228) AND asystole: epinephrine administered</p>		<p>neurological outcome.</p> <p>Epinephrine administered asystole patients were more likely than control patients to have survive as well as have a greater neurological outcome.</p> <p>Epinephrine more effective for those with initial PEA than those with initial asystole.</p>	<p>Could not consider treatment after arrival to hospital due to database only including prehospital information.</p> <p>Did not consider epinephrine doses.</p> <p>Outcomes of study were not evaluated at the same point in time; the outcomes at 1 month or at discharge, whichever earlier, were recorded in the data base. Might cause an overestimation of the outcome.</p> <p>Addressed only OHCA patients with witnessed arrest as in Japan epinephrine is not generally recommended for unwitnessed patients with initial asystole.</p>
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		(n=10816) or no epinephrine (n=54949).			
<p>Title:</p> <p>A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest</p> <p>Authors:</p> <p>G.D. Perkins, C. Ji, C.D. Deakin, T. Quinn, J.P. Nolan, C. Scomparin, S. Regan, J. Long, A. Slowther, H. Pocock, J.J.M. Black, F. Moore, R.T. Fothergill, N. Rees, L. O’Shea, M. Docherty, I. Gunson, K. Han, K. Charlton, J. Finn,</p>	<p>Study Design:</p> <p>The study was a randomized double blind trial involving patients with out-of-hospital cardiac arrest in the United Kingdom.</p> <p>Patients either received parenteral epinephrine or saline placebo along with standard care.</p> <p>The study took place from December 2014 through October 2017.</p> <p>Question/Purpose:</p> <p>To measure the effectiveness of epinephrine administration in OHCA.</p>	<p>Inclusion Criteria:</p> <p>Inclusion criteria was adult patients (16+) who had sustained an out-of-hospital cardiac arrest for which advanced life support was provided by trial-trained paramedics.</p> <p>Exclusion Criteria:</p> <p>Exclusion criteria was known or apparent pregnancy, an age less than 16 years, cardiac arrest from anaphylaxis or asthma, or the administration of epinephrine before</p>	<p>Measured Variables:</p> <p>Age, sex, initial cardiac rhythm, cause of cardiac arrest, witness of cardiac arrest and whom CPR was performed by.</p> <p>Primary:</p> <p>The primary outcome was the rate of survival at 30 days.</p> <p>Secondary:</p> <p>The secondary outcomes were the rate of survival until hospital admissions, the lengths of stay in the hospital and in the intensive care unit, the rates of survival at hospital discharge and at 3 months and the</p>	<p>Results:</p> <p>36.3% had a ROSC among epinephrine group in comparison to 11.7% has a ROSC in the placebo group.</p> <p>At 30 days, 3.2 % survived among the epinephrine group.</p> <p>At 30 days, 2.4% survived in the placebo group.</p> <p>Favorable Neurological outcome at the time of discharge: 2.2% among epinephrine group and 1.9% among placebo group. However, severe neurological</p>	<p>Strengths:</p> <p>Characteristics similar among epinephrine and placebo groups.</p> <p>Large sample size (n=8016).</p> <p>Similar test size groups: epinephrine (n=4012) and placebo (n=3995).</p> <p>Assignment of participants to interventions was randomized and double blinded.</p> <p>Weaknesses:</p> <p>Only age (16+).</p> <p>Limitations:</p>

<p>S. Petrou, N. Stallard, S. Gates, and R. Lall, for the PARAMEDIC2 Collaborators</p> <p>Year Published:</p> <p>2018</p>	<p>Specifically, to determine whether epinephrine is beneficial or harmful as a treatment in OHCA.</p> <p>LOE - II</p>	<p>the arrival of the trial-trained paramedic.</p> <p>Total Population:</p> <p>N=10623 patients assessed for eligibility.</p> <p>After exclusion criteria there was <u>n = 8016</u> enrolled in the trial with n=3995 receiving placebo in the primary analysis and n=4012 receiving epinephrin in the primary analysis.</p>	<p>neurological outcomes at hospital discharge and at 3 months.</p>	<p>impairment was more common in the epinephrine group than the placebo group.</p> <p>Survival at 3 months and neurological outcomes at 3 months were similar among the 2 groups.</p>	<p>Used same dosage whereas differential dosage may exhibit different results.</p> <p>Earlier administration of epinephrine may have influenced the result.</p> <p>Not enough information was collected about the patient's initial neurological function before cardiac arrest.</p>
<p>Title:</p> <p>Favorable neurological outcomes by early epinephrine administration within 19 minutes after</p>	<p>Study Design:</p> <p>The study design is a nationwide, prospective, population-based observational study. They looked at witnessed cardiac</p>	<p>Inclusion Criteria:</p> <p>Patients aged 15 to 89 who had witnessed cardiac arrests. From there they were either administered epinephrine or not.</p>	<p>Measured Variables:</p> <p>Sex, age, type of bystander, witness status, initial ECG rhythm, elapsed time intervals during resuscitation, type of</p>	<p>Results:</p> <p>ROSC was seen in 18% of the epinephrine group and 9.4% in the non-epinephrine group.</p>	<p>Strengths:</p> <p>Clear and focused question.</p> <p>Large sample size (n=119639)</p> <p>Similar age and sex characteristics</p>

<p>EMS call for out-of-hospital cardiac arrest patients</p> <p>Authors:</p> <p>H. Tanaka, H. Takyu, R. Sagisaka, H. Ueta, Toru Shirakawa, Tomoya Kinoshi, Hiroyuki Takahashi, Takashi Nakagawa, Syuji Shimazaki and M. Ong Eng Hock</p> <p>Year Published:</p> <p>2016</p>	<p>arrests from 2008 to 2012.</p> <p>Question/Purpose:</p> <p>The aim of the study was to evaluate time dependent effect of the early administration of epinephrine within 19 minutes after EMS call on neurological outcomes at 1 month in patients with OHCA.</p> <p>LOE - IV</p>	<p>Exclusion Criteria:</p> <p>Subjects were excluded from the study if missing initial rhythm, unknown bystander-initiated CPR, unknown CPC, unknown airway management device, outlying response time data, and ROSC before EMS arrival, unknown drug administration and drug administered post ROSC.</p> <p>Cases where ROSC was achieved within 2 minutes after PAD by a layperson or EMS defibrillation excluded because these patients would not require epinephrine. 2</p>	<p>bystander-initiated CPR, type of advanced airway management, IV fluids, and EPI administration, as well as prehospital ROSC, 1-month survival, and neurological status at one month after the event.</p> <p>Primary:</p> <p>The primary outcome was CPC 1-2 at 1 month after collapse.</p> <p>Secondary:</p> <p>The secondary outcome was field ROSC among the two groups.</p>	<p>A favorable neurological outcome was achieved in 5.2% in non-epinephrine group and 2.9% in the epinephrine group.</p> <p>ROSC was seen in 24.8% among the early epinephrine group, 18.9% in the intermediate epinephrine group, 14.7% in the late epinephrine group and 11.5% in the very late epinephrine group.</p> <p>A favourable neurological outcome was seen in 5.7% in the early epinephrine group, 2.9% in the intermediate epinephrine group, 1.5% in the late epinephrine group and 1.6% in the</p>	<p>among the two groups.</p> <p>Lengthy review period (4 years).</p> <p>Included time dependent factor in effectiveness of epinephrine.</p> <p>Looked at airway management during OHCA.</p> <p>Weaknesses:</p> <p>Large difference in sample sizes between epinephrine group (n=20420) and no epinephrine (n=99219). Only ages (15+).</p> <p>Limitations:</p> <p>Based on a retrospective cohort analysis and not a randomized controlled study.</p>
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		<p>patients were excluded because there was less than a 5-minute time frame between 119 call and epinephrine administration.</p> <p>Total Population:</p> <p>Before exclusion there was n = 925288 patients with OHCA within those dates.</p> <p>Eligible patients after exclusion were <u>n = 119639</u>.</p> <p>These were then split into epinephrine administered (n=20420) and no-epinephrine administered (n=99219)</p> <p>The epinephrine administered group</p>		<p>very late epinephrine group.</p>	<p>Cannot control confounding factors: airway devices, failure to obtain IV access, variation of skills.</p> <p>Nothing on outcome in hospital which may influence survival outcome.</p> <p>Quality of CPR not recorded.</p>
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		was then split dependent on the time epinephrine was administered: early EPI (5-18 min), intermediate EPI (19-23 min), late EPI (24-29 min), and very late EPI (30-62 min)			
<p>Title:</p> <p>Effect of Prehospital Epinephrine Use on Survival from Out-of-Hospital Cardiac Arrest and on Emergency Medical Services</p> <p>Authors:</p> <p>Song Yi Park, Daesung Lim, Seong Chun Kim, Ji Ho Ryu, Yong Hwan Kim, Byungho Choi and Sun Hyu Kim</p>	<p>Study Design:</p> <p>The study design was a retrospective observational study.</p> <p>The researchers looked at two groups: epinephrine administration and non-epinephrine usage during OHCA.</p> <p>Data collection took place over two different timelines. The first data collection was from November 1, 2019, to January 31, 2020. The second data collection was from November</p>	<p>Inclusion Criteria:</p> <p>All patients for whom resuscitation was attempted by EMS providers due to OHCA during the study periods were included in the study.</p> <p>Exclusion Criteria:</p> <p>The exclusion criteria were if the patient was less than 18 years old, obvious death, DNA, trauma cardiac arrest,</p>	<p>Measured Variables:</p> <p>Age, sex, and medical history.</p> <p>Data for the EMS variables of the presence of an initial shockable rhythm on the scene, the use of advanced airway management, the use of mechanical chest compression devices, the use of epinephrine, and EMS process time.</p> <p>Data for the hospital variables of ROSC at any time, survival to discharge and favorable neurological</p>	<p>Results:</p> <p>Survival to discharge rate of epinephrine group was 5% in total population and 4.7% in the 1-1 matched population.</p> <p>Favorable neurological outcomes of epinephrine group was 3.6% in total population and 3.1% in the 1-1 matched population.</p> <p>None of the results above were</p>	<p>Strengths:</p> <p>Compared two different study periods pre and post COVID-19.</p> <p>1-1 propensity matched.</p> <p>Looked at airway management during OHCA.</p> <p>Weaknesses:</p> <p>Slightly smaller sample size (n=1949).</p> <p>Difference in sample sizes between tests groups: epinephrine</p>

<p>Year Published:</p> <p>2021</p>	<p>1, 2020, to January 31, 2021.</p> <p>Question/Purpose:</p> <p>The purpose was to identify the effect of epinephrine in the survival of OHCA patients as well as changes in the prehospital EMS after the introduction of prehospital epinephrine use by EMS providers.</p> <p>LOE – IV</p>	<p>intoxication and drowning.</p> <p>As well, patients were excluded due to events that occurred in the healthcare facility, duplicated data, missing data, refusal to provide hospital data and absence of data on epinephrine.</p> <p>Total Population:</p> <p>N=2884 OHCA patients were eligible to be included during the study period.</p> <p>After, exclusion criteria <u>n=1949</u> were included in the study population.</p> <p>N=337 were in the epinephrine group and n=1612 were</p>	<p>outcome were collected.</p> <p>Primary:</p> <p>The primary outcome of the study was the survival to discharge and favorable neurological outcomes of OHCA patients.</p> <p>Secondary:</p> <p>The secondary outcomes were the change in the prehospital EMS after the introduction of prehospital epinephrine use by EMS providers.</p>	<p>statistically significant.</p> <p>Initial shockable rhythm rate of survival to discharge was 23.8%</p> <p>Initial no shockable rhythm rate of survival was 1.8%. Epinephrine group received more mechanical chest compression, longer EMA response times and longer scene times than norepinephrine group.</p> <p>Mechanical chest compression was a negative prognostic factor for survival to discharge and favorable neurological outcomes in epinephrine group.</p>	<p>(n=337) and no epinephrine (n=1612).</p> <p>Only medical arrests, no trauma.</p> <p>Only adults (18+).</p> <p>Limitations:</p> <p>Detailed in-hospital treatment of post-cardiac arrest care was not considered.</p> <p>Frequency of epinephrine usage was not analyzed.</p> <p>Mechanical chest compression devices were more commonly used in the epinephrine group and the use of them were related to a poor prognosis in the study.</p>
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		in the non-epinephrine group.			
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Comments:

Overall results from each article in the order they were presented in the chart above:

Both survival to hospital discharge and favorable neurological outcome was statistically significant in time dependent epinephrine administration.

Over the four-year review epinephrine usage increased every progressing year. Epinephrine is linked to increasing ROSC among patients that initially present in a non-shockable rhythm. Patients presenting in PEA who received epinephrine had a higher chance of survival than the control patients, but there were no differences between the groups on overall neurological outcome. Patients presenting in asystole and received epinephrine had both a higher rate of survival and overall favorable neurological outcome compared to control group.

Greater chance of ROSC in OHCA among epinephrine group compared to placebo group. Neurological impairment was more common among the epinephrine group than the placebo group.

Higher rate of ROSC among the epinephrine group than those who did not receive epinephrine. There was greater neurological outcome in those who did not receive epinephrine than those who had epinephrine administered. The faster epinephrine is administered (especially between 5-18 minutes upon arrival) is linked to the greatest chance of ROSC and favorable neurological outcomes.

Found there was no significant enhancement in the survival to discharge of OHCA patients or favorable neurological outcomes among those who received epinephrine.

Considerations:

Discussed below are some considerations to think about when attempting to use the evidence outlined in the review.

For starters each of the studies used what they defined as an adult population and the affects epinephrine had on ROSC, survival rate

or favorable neurological outcomes. For example, the study done by Tanaka et al. (2016), used patients 15 years old and above whereas, Park et al. (2021), used by patients 18 years old and above. In total, the review had an age range of 15-94 years of range. Therefore, some study populations defined adult at a younger age than other studies which may influence the results. In addition, no pediatric samples were examined, thus the results from these studies cannot be generalized to the pediatric patient as epinephrine administration may elicit a different effect on such population.

Total sample size should be considered while examining the review due to the variation in sample size among the studies that were reviewed. A benefit of the studies chosen is that they all had large sample sizes, but they did vary in how large they were. It is often considered that the larger the sample size the more reliable the evidence may be but is there a point where a sample size is too large. In this review the sample sizes were: 41 079, 110 239, 8016, 119 639 and 1949. Thus, that is a variable range from a study population from close to 2000 all the way to above 100 000 patients.

There were different locations for each the studies which raises some considerations. Two of the studies were completed in Japan, one in the United Kingdom, one across North America and one in Busan, Ulsan, Gyeongnam and Changwon (along coast of southeastern part of Korea). Somethings to consider among each location is the population size, differing protocols among emergency services which could affect the generalizability of the results and the review.

Clinical bottom line:

Based on the evidence found from the review there cannot be a definitive answer to the question at hand: In the prehospital setting does the usage of epinephrine versus no epinephrine result in an increased patient outcome and a higher chance of getting a ROSC among OHCA patients?

OHCA patients have a heightened chance of ROSC if epinephrine is administered than if not administered. Specifically, the faster epinephrine is administered to OHCA patient upon arrival (5-18 minutes) is linked to increased ROSC.

There was a greater risk of neurological related problems in those that received epinephrine and favorable neurological outcomes in those that did not receive epinephrine in majority of the articles in this review.

Although, evidence is provided that epinephrine administration in OHCA leads to greater chance of ROSC among patients, it is unknown whether the ROSC benefits outweigh neurological complications.

References

Okubo, M., Komukai, S., Callaway, C. W., & Izawa, J. (2021). Association of timing of epinephrine administration with outcomes in adults with out-of-hospital cardiac arrest. *JAMA Network Open*, 4(8), 1–14. <https://doi.org/10.1001/jamanetworkopen.2021.20176>

Park, S.Y., Lim, D., Kim, S.C., Ryu, J.H., Kim, Y.H., Choi, B., Kim, S.H. (2022). Effect of Prehospital Epinephrine Use on Survival from Out-of-Hospital Cardiac Arrest and on Emergency Medical Services. *Journal of Clinical Medicine*, 11(190), 1 – 13. <https://doi.org/10.3390/jcm11010190>

Perkins, G. D., Lall, R., Gates, S., Stallard, N., Petrou, S., Finn, J., Han, K., Gunson, I., Docherty, M., O'Shea, L., Rees, N., Fothergill, R. T., Moore, F., Black, J., Pocock, H., Slowther, A., Long, J., Regan, S., Scomparin, C., ... Deakin, C. (2018). A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest . *The New England Journal of Medicine*, 379(8), 711–721. <https://doi.org/10.1056/NEJMoa1806842>

Tanaka, H., Takyu, H., Sagisaka, R., Ueta, H., Shirakawa, T., Kinoshi, T., Takahashi, H., Nakagawa, T., Shimazaki, S., & Ong Eng Hock, M. (2016). Favorable neurological outcomes by early epinephrine administration within 19 minutes after EMS call for out-of-hospital cardiac arrest patients. *The American Journal of Emergency Medicine*, 34(12), 2284–2290. <https://doi.org/10.1016/j.ajem.2016.08.026>

Tomio, J., Nakahara, S., Takahashi, H., Ichikawa, M., Nishida, M., Morimura, N., & Sakamoto, T. (2017). Effectiveness of Prehospital Epinephrine administration in improving long-term outcomes of witnessed out-of-hospital cardiac arrest patients with initial non-shockable rhythms. *Prehospital Emergency Care*, 21(4), 432–441. <https://doi.org/10.1080/10903127.2016.1274347>

Appendix



Searching: [CINAHL Plus with Full Text](#) | [Choose Databases](#)

prehospital or pre hospital or pre-hospital or out of Select a Field (optional) ▾ Search

AND ▾ epinephrine or adrenaline Select a Field (optional) ▾ Clear ?

AND ▾ cardiac arrest or heart arrest or cardiopulmc Select a Field (optional) ▾ + -



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Search ID#	Search Terms	Search Options	Actions
<input type="checkbox"/> S3	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Limiters - Full Text; Published Date: 20160101-20221231 Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (14) View Details Edit
<input type="checkbox"/> S2	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Limiters - Published Date: 20160101-20221231 Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (198) View Details Edit
<input type="checkbox"/> S1	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (419) View Details Edit



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prehospital or pre hospital or pre-hospital or out of Select a Field (optional) ▾

AND ▾ epinephrine or adrenaline Select a Field (optional) ▾

AND ▾ cardiac arrest or heart arrest or cardiopulm Select a Field (optional) ▾

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Search ID#	Search Terms	Search Options	Actions		
<input type="checkbox"/> S3	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Limiters - Linked Full Text; Date of Publication: 20160101-20221231 Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (38)	View Details	Edit
<input type="checkbox"/> S2	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Limiters - Linked Full Text Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (66)	View Details	Edit
<input type="checkbox"/> S1	(prehospital or pre hospital or pre-hospital or out of hospital or non hospital setting or prehospital care or emergency medical services or prehospital service) AND (epinephrine or adrenaline) AND (cardiac arrest or heart arrest or cardiopulmonary arrest)	Expanders - Apply related words; Apply equivalent subjects Search modes - Find all my search terms	View Results (771)	View Details	Edit