

**A race against time: Does Epinephrine compliance by emergency
physicians increase ROSC in cardiac arrest patients**

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Main Document

Abstract: One of the most crucial medicinal intervention during a cardiac arrest is epinephrine. Advanced cardiac life support (ACLS) guidelines lays out the recommendation of delivering epinephrine every 3 – 5 minutes. The purpose of this study is to evaluate if physicians are compliant with delivering epinephrine as recommended, and how does compliance vs. non-compliance affect patient outcomes as measured by attaining return of spontaneous circulation (ROSC). The design of this study is a retrospective chart review with analysis, using Wilcox-Rank sum and Chi-Square fisher exact test to evaluate for statistical significance, which was defined with a P value < 0.05. There were 111 patient charts included in the study, and the results were charted into 3 categories: demographics by non-compliance, any non-compliance and mean non-compliance, and demographics by sinus rhythm. None of the results showed any statistical significance except for the mean number of doses a patient receives to achieve sinus rhythm, which was a mean of 10.3 vs 3.95. Although this study did not achieve statistical significance overall, it highlighted some clinical significance that may be of importance moving forward for all physicians. One clinical aspect that this study highlights further is the health disparity that people of color encounter. Patients who are people of color experienced higher mean number of non-compliance and percentage of any non-compliance. The overall conclusion that this study emphasized is that more studies into the overall quantity of epinephrine given during resuscitation may be worthwhile. Additionally, further emphasis on the importance of physician awareness of health disparity among people of color is needed.

Objectives: The rationale behind this scholarly project is that there are many moving variables during a cardiac resuscitation effort, and it is imperative that ACLS standards are implemented in a timely manner. The significance of this project is that it will provide concrete data to HonorHealth John C. Lincoln Medical Center, allowing physicians to see what the current adherence rate is with epinephrine delivery during a cardiac arrest.

Main Document

Additionally, this project may allow us to evaluate the significance of epinephrine to help achieve ROSC, and its effect on survival to admission from cardiac arrest.

Methods:

Research question and Hypothesis

Do patients who receive epinephrine at intervals recommended by the AHA ACLS Guidelines during cardiac resuscitation efforts by emergency physicians have higher rates of ROSC and ICU admissions? Since epinephrine is mainly used for its adrenergic effects, this may increase the likelihood of achieving adequate coronary perfusion to achieve ROSC, then administering Epinephrine every 3 - 5 minutes should increase the possibility of successful ROSC.

Study setting and patients

The study took place in Phoenix, Arizona, hometown to an approximate 1,680,992 people with an estimate of 55.1% of adults over the age of 18 and within the 55.1%, 8.4% are adults over the age of 65⁹. There are 24 hospitals serving the metropolitan Phoenix area, one of these hospitals is HonorHealth John C. Lincoln Medical Center where it sees an estimate of 800 cardiac arrests per year. HonorHealth John C. Lincoln will be where this study takes place. We will review all patients with an ICD-9 code of 427.5, 799.1, and ICD-10 code of I46.2, I46.8, I46.9, and R09.2 in the electronic health record at HonorHealth John C. Lincoln Medical Center between August 2012 – January 2018. All patients who are 18 years and older will be evaluated. Exclusion criteria include pediatric patients age less than 18 years, presenting as trauma in cardiac arrest, patients who received vasopressin other than epinephrine, and in-patient cardiac arrests.

Study Design

Once the appropriate patients have been identified, multiple criteria's will be evaluated. In order to be considered in compliance with ACLS standards, epinephrine must be delivered IV or IO (intraosseous) with an average time of 3 – 5 minutes during the

Main Document

course of resuscitation efforts in the emergency department. An average time that is less than 3 minutes or greater than 5 minutes will be considered non-compliant. We will evaluate the quantity of ROSC, survival to admission, and patient demographics to assess for patients who receive epinephrine consistently with an average time between 3 – 5 minutes and compare to patients who fall under the non-compliant category. Additionally, EPIC (EMR) provides documentation down to the second; therefore, any epinephrine given at a minute mark between 0-30 seconds will be rounded down, and epinephrine given between 31-59 seconds will be rounded up to the next minute. For example: epinephrine given at 3 minutes and 30 seconds will be rounded down to 3 minutes; whereas epinephrine given at 3 minutes and 31 seconds will be rounded up to 4 minutes. Also, if EKG data is available, it will be collected to document the patient's initial rhythm either prior to arrest or the rhythm at arrest. IRB was obtained for this study and was exempt.

Study outcome

The primary outcome of this study is to achieve ROSC while in the emergency department during cardiac resuscitation and to evaluate for the number of times a patient may achieve ROSC over a course of resuscitation efforts. A secondary outcome is to conduct a sub-group analysis comparing patients within the compliant vs. non-compliant groups to evaluate for health disparity among non-Caucasian patients.

Risks and Benefits

Risks: There will be no direct patient contact. Minor risk is loss of patient confidentiality, but measures will be taken to minimize that risk including de-identification of data, password protected database, and limited access to only research team members.

Benefits: There will be no direct benefits to the patients involved in this study.

Methods and Measurements

Pharmacy staff and our study team will retrieve data on cardiac arrest patients from HonorHealth John C. Lincoln Medical Center. Physical barriers to protect hard copy data will

Main Document

be locked in a cabinet behind a locked door in the emergency department if needed.

Electronic data will be stored within the HonorHealth network behind their firewall, which will be protected by a lengthy password. Data will be analyzed concurrently with Paul Kang, MPH, Statistician, at the University of Arizona College of Medicine – Phoenix.

Variables

Independent variables that we will evaluate include:

- Age
- Gender
- Race
- Number of doses
- Route of delivery

Dependent variables that we will evaluate include:

- ROSC in the ED
- Number of sinus rhythm attained

Power and Sample Size Calculation

The primary outcome for this power and sample calculation is the proportional difference of patient who present with return of spontaneous circulation between patients who receive epinephrine consistently between 3 – 5 minutes versus those who do not. Currently, the proportions of patients who are administered epinephrine who present with return of spontaneous circulation is 5% nationally, if we expect to observe a 10% increase in the proportion of patients, then 282 (141 in each group) patients are needed to achieve a statistical power of 80%. If the difference increases to 20%, 98 (49 in each group) patients are needed to achieve a statistical power of 80%.

Statistical analysis

Main Document

Patient demographic and clinical characteristics between physician compliances vs non-compliance were reported as means, standard deviation for continuous variables and frequency, and percentages for categorical variables. The Wilcoxon rank sum was used to assess differences for continuous variables between the two groups while chi-square/Fisher exact test was used to compare categorical variables. In addition, these comparisons were made between patients with no sinus rhythm vs. patients with sinus rhythm. Finally, frequencies and percentages of any non-compliance were tallied relative to patient demographic characteristics. Furthermore, the mean number of non-compliances were assessed relative to patient characteristics. Once again, the Wilcoxon rank sum was used to assess the mean number of non-compliance relative to patient characteristics. Chi square and Fisher exact were used to compare frequency of non-compliances. All P – values were 2 sided, and a P value of <0.05 was considered statistically significant. All data analysis was used by STATA version 15 (College Station, Texas).

Results: The first table evaluates emergency physician's compliance with epinephrine delivery during cardiac resuscitation, which was broken down into multiple categorical variables including patients: age, male gender, non-Caucasian race, and route. Whereas ordinal variables were broken down into number of doses and number of times sinus rhythm was achieved.

This chart demonstrated that the average age for the patient population evaluated was 62.7 years of age. Sixty-seven patients out of 111 were male patients. Forty out of 111 physicians were compliant based on ACLS guidance definition, and 71 were not based on the cut off criteria established for this study. One clinically significant stand out is that out of all 40 physicians who were compliant with ACLS guidelines, none of the patients ever achieved sinus rhythm. On the contrary, of the 71 physicians who fell within the non-compliant criteria, three of these physicians were able to achieve sinus rhythm at least

once. Specifically, two of the patients had a sinus rhythm once, and the last patient achieved sinus rhythm twice.

This chart demonstrated that all P values were greater than 0.05, indicating that there was no statistical significance between compliant and non-compliant physicians during cardiac resuscitation efforts. However, analysis of other variables indicated there may be a clinical significance, despite not having any statistical significance in the next two charts.

Demographics by non-compliance (Table 1)

| Variables | Overall N=111 | Compliant N=40 | Any Non- compliance N=71 | p- value |
|-------------------------------|------------------|-------------------|--------------------------------|-------------|
| Age, years (mean, SD) | 62.7 (15.6) | 61.5 (15.5) | 63.4 (15.9) | 0.58 |
| Sex (male, %) | 67 (60.4) | 27 (67.5) | 40 (56.3) | 0.25 |
| Race, non-Caucasian (n, %) | 22 (19.8) | 6 (15.0) | 16 (22.5) | 0.34 |
| Number of Doses (mean, SD) | 4.12 (2.55) | 4.50 (2.26) | 3.91 (2.69) | 0.12 |
| Route (n, %) | | | | 1.0 |
| IO | 8 (7.21) | 3 (7.50) | 5 (7.04) | |
| IV | 100 (90.1) | 36 (90.0) | 64 (90.1) | |
| Both/Other | 3 (2.70) | 1 (2.50) | 2 (2.82) | |
| # of Sinus Rhythm (n, %) | | | | 0.18 |
| 0 | 108 (97.3) | 40 (100.0) | 68 (95.8) | |
| 1 | 2 (1.80) | | 2 (2.82) | |
| 2 | 1 (0.90) | | 1 (13.41) | |

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The next chart evaluates any non-compliance and mean non-compliance. When evaluating any non-compliance, in essence if a physician met criteria for non-compliance at least one time during the course of resuscitation efforts, it will fall under non-compliant for this chart. Looking at demographics of patients, 22 out of 35 patients were less than 55 years of age fell into the any non-compliance category. There were 39 patients who were age 55 and older, but under 70, where 23 of these patients fell under the any non-compliance category. Lastly, there were 37 patients aged 70 and over, and of the 37 there were 26 patients that fell under the any non-compliance category.

One interesting revelation of this chart is under race. There was a total of 89 Caucasian patients, and 55 of them fell under the any non-compliance group. The non-Caucasian group had a total of 22 patients, where 16 fell under the any non-compliance group. Both groups did not meet any statistical significance. However, the frequency represented in parenthesis next to their respective numbers, and evaluating the mean non-compliance for these two groups show that non-Caucasian groups experience an overall greater chance of non-compliance during resuscitation. Again, this does not meet statistical significance, but may be clinically significant, that further highlights the healthy disparity that non-Caucasian patients experience in the healthcare system. Lastly, evaluating the mean number of non-compliance in regards to the number of doses of epinephrine delivered showed that when only 1-2 doses are delivered, the mean number of non-compliance is greater compared to when 5 or more doses are delivered. However, the P value is still greater than 0.05, suggesting that there is no statistical significance.

Any non-compliance and mean noncompliance (Table 2)

| Variables | Any Non-compliance | p-value | Mean Number of Non-compliances | p-value |
|------------|--------------------|---------|--------------------------------|---------|
| Age, years | | 0.58 | | 0.56 |

Main Document

| | | | | |
|----------------------|-----------|------|-------------|------|
| < 55 (n=35) | 22 (62.8) | | 1.14 (1.28) | |
| ≥55-< 70 (n=39) | 23 (58.9) | | 1.05 (1.19) | |
| ≥70 (n=37) | 26 (70.3) | | 1.35 (1.35) | |
| Sex | | 0.25 | | 0.93 |
| Female (n=44) | 31 (70.5) | | 1.09 (1.12) | |
| Male (n=67) | 40 (59.7) | | 1.24 (1.37) | |
| Race | | 0.34 | | 0.13 |
| Caucasian (n=89) | 55 (61.8) | | 1.09 (1.23) | |
| Non-Caucasian (n=22) | 16 (72.7) | | 1.54 (1.40) | |
| Number of Doses | | 0.35 | | 0.09 |
| 1-2 (n=31) | 23 (74.2) | | 1.64 (1.58) | |
| 3-4 (n=42) | 26 (61.9) | | 1.14 (1.24) | |
| ≥5 (n=38) | 22 (57.9) | | 0.84 (0.88) | |
| Route | | 1.0 | | 0.69 |
| IO (n=8) | 5 (62.5) | | 1.75 (2.05) | |
| IV (n=100) | 64 (64.0) | | 1.13 (1.20) | |
| Both/Other (n=3) | 2 (66.7) | | 1.33 (1.15) | |
| # of Sinus Rhythm | | 0.70 | | 0.34 |
| 0 (n=108) | 68 (62.9) | | 1.16 (1.27) | |
| 1 (n=2) | 2 (100.0) | | 1 (0) | |
| 2 (n=1) | 1 (100.0) | | 3 (N/A) | |

The last chart assessed demographics by sinus rhythm, which means it came down to each respective category of either achieving sinus rhythm by a simple yes or no comparison. Again, all of these categories did not meet statistical significance, except for one, which was the number of doses of epinephrine delivered. For patients who did not achieve any sinus rhythm during the course of resuscitation, the mean number of doses

Main Document

delivered was 3.95. Compared to the three patients who did achieve sinus rhythm, the mean number of doses delivered was 10.3, with a P value of 0.04. This meets statistical significance, and may also indicate a clinical significance that more epinephrine delivered may help achieve ROSC.

Demographics by Sinus Rhythm (Table 3)

| Variables | No Sinus Rhythm N=108 | Sinus Rhythm N=3 | p-value |
|--------------------------------------|--------------------------|---------------------|---------|
| Age, years (mean, SD) | 62.3 (15.5) | 77.6 (21.9) | 0.18 |
| Sex (male, %) | 66 (61.1) | 1 (33.3) | 0.56 |
| Race, non-Caucasian (n, %) | 22 (20.4) | 3 (100.0) | 1.0 |
| Number of Doses (mean, SD) | 3.95 (2.06) | 10.3 (8.38) | 0.04 |
| Route (n, %) | | | 1.0 |
| IO | 8 (7.41) | | |
| IV | 97 (89.8) | 3 (100.0) | |
| Both/Other | 3 (2.78) | | |
| Any Non-Compliance (yes, %) | 68 (62.9) | 3 (100.0) | 0.55 |
| Number of Non-compliances (mean, SD) | 1.17 (1.27) | 1.67 (1.15) | 0.34 |

Conclusions: Unfortunately, this study did not yield the results that we were hoping for. Overall study did not show if epinephrine compliance actually affected the outcome for patients in cardiac arrest. However, it is important to note that there was some statistical significance in regards to the number of epinephrine doses given. Additionally, even though the overall study

did not reach statistical significance, there may be strong clinical significance in regards to health disparity

Introduction

Epinephrine has been known to be available for over 100 years. It has been consistently used for cardiac arrests since 1960's after it showed return of spontaneous circulation (ROSC) in animal studies ¹. Cardiopulmonary resuscitation, along with epinephrine has been at the core of advanced cardiac life support (ACLS) standards, though changes have occurred throughout the years ². Gueugniaud, et al, conducted a study that looked at repeated doses of high dose epinephrine (5mg) versus standard dose (1mg) for out of hospital cardiac arrest patients ³. Based on their study, repeat high dose epinephrine had 40.4% patients with ROSC compared to 36.4% for standard dose. In regards to survival to admission, high dose epinephrine had 26.5% patients admitted, whereas standard dose had 23.6% admitted ³. However, when it came to in-hospital mortality, the high dose group had a higher rate at 38.7% compared to 32.4%; and high dose epinephrine did not improve survival to discharge or neurological functionality ³. Consequently, standard dose of epinephrine is still recommended compared to high dose epinephrine.

Although epinephrine has been utilized for many decades, its effects has not been evaluated in any clinically randomized trials due to ethical concerns. Donnino, et al, conducted a retrospective study at 570 hospitals between 2000 – 2009 to evaluate the effectiveness of epinephrine on non-shockable (asystole and pulseless electrical activity) cardiac arrest patients ⁴. The second criteria the study looked at was the timing of when the initial dose of epinephrine was given. From the 570 hospitals, there were 119,978 cases of cardiac arrests where 55% were asystole and 45% were in pulseless electrical activity, which means these patients were candidates for epinephrine and CPR only. Of note, only 25,095 patients met the studies' criteria, as the remaining patients from the total of

Main Document

119,978 were excluded based on the studies' exclusion criteria ⁴. Based on Donnino's study, the median time to the initial dose of epinephrine was 3 minutes for in-hospital cardiac arrests. There was a decrease in survivability with each increasing interval of time to the first dose of epinephrine, where each interval was set at 3 minutes. Of the 25,095 patients, 12,215 patients sustained ROSC (49%), 6,820 survived to 24 hours (27%), and 2,603 survived to hospital discharge (10%) ⁴. Based on a limited of studies, it can be noted that epinephrine's role as an adrenaline helps achieve ROSC, but its side effects has yet to be fully evaluated.

ACLS' 2015 updated guidelines evaluated a study that looked at short term and long-term outcomes with standard epinephrine doses versus placebo. Standard dose of epinephrine is defined as 1mg IV/IO every 3 – 5 minutes. This study that the ACLS evaluated was determined to be underpowered with a sample size of 500 ⁵. However, the ACLS concluded that there was an improvement in ROSC with standard epinephrine delivery, though there are conflicting results when compared to observational studies. At this time, the ACLS recommends with a Class IIb classification of delivering epinephrine every 3 – 5 minutes ⁶. However, it is important to consider that ACLS highlighted that giving epinephrine is only deemed a "may be reasonable" treatment, and that the "usefulness/effectiveness is unclear" ⁶.

On the flip side, Scliopou's team performed an observational study to evaluate paramedic's ACLS adherence for out of hospital cardiac arrest patients. Their study was a retrospective analysis of all cardiac arrest patients between February 2004 to October 2005 from the EMSCQI (Emergency Medical Services Continuous Quality Improvement) database. Scliopou, et al, determined that non-compliance was when epinephrine was given less than 3 minutes or greater than 5 minutes ⁷. The research team found 75 patients out of 11,000 to be considered out of hospital cardiac arrest, where the average time to receiving the first dose of Epinephrine was 22.6 minutes ⁷. Lastly, the team concluded that only 14% out of hospital cardiac arrest patients received epinephrine according to ACLS guidelines ⁷.

Main Document

When it comes to physician compliance with delivering epinephrine, Draper and Eppert conducted a retrospective analysis in 2008 to assess compliance of ACLS standards during cardiopulmonary resuscitation efforts in a community teaching hospital. The research team evaluated 74 cardiac arrest patients between January 1st 2003 – June 30th 2004. Non-compliance fell into multiple categories including: incorrect medication dosage, delayed sequential treatment, omission of indicated treatment, deviation from recommended guidelines, and incorrect energy for defibrillation ⁸. Of the 14 cases where incorrect dosage of medication was given, six of those pertained to incorrect epinephrine dosage ⁸. Eight non-compliant cases fell under the omission branch, four of those cases involved epinephrine being omitted. Eleven cases documented a delay in delivering the appropriate treatment, seven of those were epinephrine. Thirteen cases deviated from the recommended guidelines, ten of those were epinephrine. The overall non-compliance rate was 58.1% for any reason, but specifically for any deviations related to epinephrine, there were 23 cases as mentioned above which came out to a 31% non-compliance ⁸. Based on Draper and Epperts retrospective study in 2008, it showed a high non-compliance rate during resuscitation efforts all around, but also shockingly high when focused on strictly delivering epinephrine.

Methods – the manuscript should be blinded **for institution and location** as well as authors, as those will often reveal authorship

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| <p>Study Design – IRB was obtained and was exempted for this study Study Setting and Population - The study took place in Phoenix, Arizona, hometown to an approximate 1,680,992 people with an estimate of 55.1% of adults over the age of 18 Study Protocol - retrospective chart review Measures – ROSC during cardiac resuscitation Data Analysis - Means, standard deviation for continuous variables and frequency, and percentages for categorical variables. The Wilcoxon rank sum was used to assess differences for continuous variables between the two groups while chi-square/fisher exact test was used to compare categorical variables. P value of less than 0.05 was established to detect statistic significance</p> |
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Results

The first table evaluates emergency physician's compliance with epinephrine delivery during cardiac resuscitation, which was broken down into multiple categorical variables including patients: age, male gender, non-Caucasian race, and route. Whereas ordinal variables were broken down into number of doses and number of times sinus rhythm was achieved.

This chart demonstrated that the average age for the patient population evaluated was 62.7 years of age. Sixty-seven patients out of 111 were male patients. Forty out of 111 physicians were compliant based on ACLS guidance definition, and 71 were not based on the cut off criteria established for this study. One clinically significant stand out is that out of all 40 physicians who were compliant with ACLS guidelines, none of the patients ever achieved sinus rhythm. On the contrary, of the 71 physicians who fell within the non-compliant criteria, three of these physicians were able to achieve sinus rhythm at least once. Specifically, two of the patients had a sinus rhythm once, and the last patient achieved sinus rhythm twice.

This chart demonstrated that all P values were greater than 0.05, indicating that there was no statistical significance between compliant and non-compliant physicians during cardiac resuscitation efforts. However, analysis of other variables indicated there may be a clinical significance, despite not having any statistical significance in the next two charts.

Demographics by non-compliance (Table 1)

| Variables | Overall N=111 | Compliant N=40 | Any Non- compliance N=71 | p- value |
|-------------------------|------------------|-------------------|--------------------------------|-------------|
| Age, years (mean, SD) | 62.7 (15.6) | 61.5 (15.5) | 63.4 (15.9) | 0.58 |
| Sex (male, %) | 67 (60.4) | 27 (67.5) | 40 (56.3) | 0.25 |
| Race, non-Caucasian (n, | 22 (19.8) | 6 (15.0) | 16 (22.5) | 0.34 |

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|-------------------------------|-------------|-------------|-------------|------|
| %) | | | | |
| Number of Doses (mean, SD) | 4.12 (2.55) | 4.50 (2.26) | 3.91 (2.69) | 0.12 |
| Route (n, %) | | | | 1.0 |
| IO | 8 (7.21) | 3 (7.50) | 5 (7.04) | |
| IV | 100 (90.1) | 36 (90.0) | 64 (90.1) | |
| Both/Other | 3 (2.70) | 1 (2.50) | 2 (2.82) | |
| # of Sinus Rhythm (n, %) | | | | 0.18 |
| 0 | 108 (97.3) | 40 (100.0) | 68 (95.8) | |
| 1 | 2 (1.80) | | 2 (2.82) | |
| 2 | 1 (0.90) | | 1 (13.41) | |

The next chart evaluates any non-compliance and mean non-compliance. When evaluating any non-compliance, in essence if a physician met criteria for non-compliance at least one time during the course of resuscitation efforts, it will fall under non-compliant for this chart. Looking at demographics of patients, 22 out of 35 patients were less than 55 years of age fell into the any non-compliance category. There were 39 patients who were age 55 and older, but under 70, where 23 of these patients fell under the any non-compliance category. Lastly, there were 37 patients aged 70 and over, and of the 37 there were 26 patients that fell under the any non-compliance category.

One interesting revelation of this chart is under race. There was a total of 89 Caucasian patients, and 55 of them fell under the any non-compliance group. The non-Caucasian group had a total of 22 patients, where 16 fell under the any non-compliance group. Both groups did not meet any statistical significance. However, the frequency represented in parenthesis next to their respective numbers, and evaluating the mean non-compliance for these two groups show that non-Caucasian groups experience an overall

Main Document

greater chance of non-compliance during resuscitation. Again, this does not meet statistical significance, but may be clinically significant, that further highlights the healthy disparity that non-Caucasian patients experience in the healthcare system. Lastly, evaluating the mean number of non-compliance in regards to the number of doses of epinephrine delivered showed that when only 1-2 doses are delivered, the mean number of non-compliance is greater compared to when 5 or more doses are delivered. However, the P value is still greater than 0.05, suggesting that there is no statistical significance.

Any non-compliance and mean noncompliance (Table 2)

| Variables | Any Non-compliance | p-value | Mean Number of Non-compliances | p-value |
|----------------------|--------------------|---------|--------------------------------|---------|
| Age, years | | 0.58 | | 0.56 |
| < 55 (n=35) | 22 (62.8) | | 1.14 (1.28) | |
| ≥55-< 70 (n=39) | 23 (58.9) | | 1.05 (1.19) | |
| ≥70 (n=37) | 26 (70.3) | | 1.35 (1.35) | |
| Sex | | 0.25 | | 0.93 |
| Female (n=44) | 31 (70.5) | | 1.09 (1.12) | |
| Male (n=67) | 40 (59.7) | | 1.24 (1.37) | |
| Race | | 0.34 | | 0.13 |
| Caucasian (n=89) | 55 (61.8) | | 1.09 (1.23) | |
| Non-Caucasian (n=22) | 16 (72.7) | | 1.54 (1.40) | |
| Number of Doses | | 0.35 | | 0.09 |
| 1-2 (n=31) | 23 (74.2) | | 1.64 (1.58) | |
| 3-4 (n=42) | 26 (61.9) | | 1.14 (1.24) | |
| ≥5 (n=38) | 22 (57.9) | | 0.84 (0.88) | |
| Route | | 1.0 | | 0.69 |

Main Document

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|-------------------|-----------|------|-------------|------|
| IO (n=8) | 5 (62.5) | | 1.75 (2.05) | |
| IV (n=100) | 64 (64.0) | | 1.13 (1.20) | |
| Both/Other (n=3) | 2 (66.7) | | 1.33 (1.15) | |
| # of Sinus Rhythm | | 0.70 | | 0.34 |
| 0 (n=108) | 68 (62.9) | | 1.16 (1.27) | |
| 1 (n=2) | 2 (100.0) | | 1 (0) | |
| 2 (n=1) | 1 (100.0) | | 3 (N/A) | |

The last chart assessed demographics by sinus rhythm, which means it came down to each respective category of either achieving sinus rhythm by a simple yes or no comparison. Again, all of these categories did not meet statistical significance, except for one, which was the number of doses of epinephrine delivered. For patients who did not achieve any sinus rhythm during the course of resuscitation, the mean number of doses delivered was 3.95. Compared to the three patients who did achieve sinus rhythm, the mean number of doses delivered was 10.3, with a P value of 0.04. This meets statistical significance, and may also indicate a clinical significance that more epinephrine delivered may help achieve ROSC.

Demographics by Sinus Rhythm (Table 3)

| Variables | No Sinus Rhythm N=108 | Sinus Rhythm N=3 | p-value |
|----------------------------|--------------------------|---------------------|---------|
| Age, years (mean, SD) | 62.3 (15.5) | 77.6 (21.9) | 0.18 |
| Sex (male, %) | 66 (61.1) | 1 (33.3) | 0.56 |
| Race, non-Caucasian (n, %) | 22 (20.4) | 3 (100.0) | 1.0 |
| Number of Doses (mean, SD) | 3.95 (2.06) | 10.3 (8.38) | 0.04 |

| | | | |
|--------------------------------------|-------------|-------------|------|
| Route (n, %) | | | 1.0 |
| IO | 8 (7.41) | | |
| IV | 97 (89.8) | 3 (100.0) | |
| Both/Other | 3 (2.78) | | |
| Any Non-Compliance (yes, %) | 68 (62.9) | 3 (100.0) | 0.55 |
| Number of Non-compliances (mean, SD) | 1.17 (1.27) | 1.67 (1.15) | 0.34 |

Discussion

In this retrospective study evaluating 111 patient charts who underwent cardiac resuscitation, the overall study suggests that delivering epinephrine in compliance with ACLS guidelines does *not* have statistical significance in restoring return of spontaneous circulation. It is also important to take into consideration that one of the main objectives was to assess physician's compliance with epinephrine delivery according to ACLS guidelines, which is highlighted to be given between a 3 – 5 minute window. From this brief study, it can be seen that there is a greater than 60% any non-compliance with epinephrine delivery during resuscitation. However, it can also be noted that although there are more physicians who fall under the any non-compliance category, this group had more patients who were able to achieve return of spontaneous circulation.

Additionally, although this study overall did not obtain any statistical significance, it is also important to evaluate if there may be any clinical significance. Based on the data obtained, it continues to highlight the health disparity that patients of color encounter. When evaluating the numbers, the mean number of non-compliance and the any non-compliance category were both substantially greater compared to Caucasian patients. Although there was a higher incidence of non-compliance among non-Caucasian patients, it is important to note that we cannot undermine the quality of care delivered from this study.

Main Document

Lastly, although we were not able to reach statistical significance, we noted that we were only a few patients shy of reaching statistical significance for categories that were of importance to us. This was one of the limiting factors for the study, where if 5-10 more patients were included, our statistician believed some areas being evaluated would have reached statistical significance. Additionally, the health disparity that was noted with the mean number of non-compliance also emphasized the ongoing socioeconomical issue faced by people of color. Also, the only statistical significance that was achieved was the number of doses given to patients who achieved sinus rhythm, which was averaged at 10.3 doses compared to 3.95 doses. This may indicate that giving more epinephrine may have a greater chance of achieving sinus rhythm, although, giving epinephrine too frequently within a short period may actually be detrimental since epinephrine is a non-specific alpha and beta agonist. This study may introduce the need to evaluate if the strong agonistic nature of epinephrine does truly cause more harm during resuscitative efforts, because if this idea is nulled, then this study may help indicate that giving more epinephrine is actually beneficial.

Limitations – Study was limited to identifying enough charts in the desired time frame to establish statistical significance

Conclusions

Unfortunately, this study did not yield the results that we were hoping for. Overall study did not show if epinephrine compliance actually affected the outcome for patients in cardiac arrest. However, it is important to note that there was some statistical significance in regards to the number of epinephrine doses given. Additionally, even though the overall study did not reach statistical significance, there may be strong clinical significance in regards to health disparity.

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Tables – Demographics by non-compliance (Table 1)

| Variables | Overall N=111 | Compliant N=40 | Any Non- compliance N=71 | p- value |
|-------------------------------|------------------|-------------------|--------------------------------|-------------|
| Age, years (mean, SD) | 62.7 (15.6) | 61.5 (15.5) | 63.4 (15.9) | 0.58 |
| Sex (male, %) | 67 (60.4) | 27 (67.5) | 40 (56.3) | 0.25 |
| Race, non-Caucasian (n, %) | 22 (19.8) | 6 (15.0) | 16 (22.5) | 0.34 |
| Number of Doses | 4.12 (2.55) | 4.50 (2.26) | 3.91 (2.69) | 0.12 |

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|--------------------------|------------|------------|-----------|------|
| (mean, SD) | | | | |
| Route (n, %) | | | | 1.0 |
| IO | 8 (7.21) | 3 (7.50) | 5 (7.04) | |
| IV | 100 (90.1) | 36 (90.0) | 64 (90.1) | |
| Both/Other | 3 (2.70) | 1 (2.50) | 2 (2.82) | |
| # of Sinus Rhythm (n, %) | | | | 0.18 |
| 0 | 108 (97.3) | 40 (100.0) | 68 (95.8) | |
| 1 | 2 (1.80) | | 2 (2.82) | |
| 2 | 1 (0.90) | | 1 (13.41) | |

Any non-compliance and mean noncompliance (Table 2)

| Variables | Any Non-compliance | p-value | Mean Number of Non-compliances | p-value |
|----------------------|--------------------|---------|--------------------------------|---------|
| Age, years | | 0.58 | | 0.56 |
| < 55 (n=35) | 22 (62.8) | | 1.14 (1.28) | |
| ≥55-< 70 (n=39) | 23 (58.9) | | 1.05 (1.19) | |
| ≥70 (n=37) | 26 (70.3) | | 1.35 (1.35) | |
| Sex | | 0.25 | | 0.93 |
| Female (n=44) | 31 (70.5) | | 1.09 (1.12) | |
| Male (n=67) | 40 (59.7) | | 1.24 (1.37) | |
| Race | | 0.34 | | 0.13 |
| Caucasian (n=89) | 55 (61.8) | | 1.09 (1.23) | |
| Non-Caucasian (n=22) | 16 (72.7) | | 1.54 (1.40) | |
| Number of Doses | | 0.35 | | 0.09 |

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|-------------------|-----------|------|-------------|------|
| 1-2 (n=31) | 23 (74.2) | | 1.64 (1.58) | |
| 3-4 (n=42) | 26 (61.9) | | 1.14 (1.24) | |
| ≥5 (n=38) | 22 (57.9) | | 0.84 (0.88) | |
| Route | | 1.0 | | 0.69 |
| IO (n=8) | 5 (62.5) | | 1.75 (2.05) | |
| IV (n=100) | 64 (64.0) | | 1.13 (1.20) | |
| Both/Other (n=3) | 2 (66.7) | | 1.33 (1.15) | |
| # of Sinus Rhythm | | 0.70 | | 0.34 |
| 0 (n=108) | 68 (62.9) | | 1.16 (1.27) | |
| 1 (n=2) | 2 (100.0) | | 1 (0) | |
| 2 (n=1) | 1 (100.0) | | 3 (N/A) | |

Demographics by Sinus Rhythm (Table 3)

| Variables | No Sinus Rhythm N=108 | Sinus Rhythm N=3 | p- value |
|----------------------------------|--------------------------|---------------------|-------------|
| Age, years (mean, SD) | 62.3 (15.5) | 77.6 (21.9) | 0.18 |
| Sex (male, %) | 66 (61.1) | 1 (33.3) | 0.56 |
| Race, non-Caucasian (n, %) | 22 (20.4) | 3 (100.0) | 1.0 |
| Number of Doses (mean, SD) | 3.95 (2.06) | 10.3 (8.38) | 0.04 |
| Route (n, %) | | | 1.0 |
| IO | 8 (7.41) | | |
| IV | 97 (89.8) | 3 (100.0) | |
| Both/Other | 3 (2.78) | | |
| Any Non-Compliance (yes, %) | 68 (62.9) | 3 (100.0) | 0.55 |
| Number of Non-compliances (mean, | 1.17 (1.27) | 1.67 (1.15) | 0.34 |

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| SD) | | | |
|-----|--|--|--|

Figure legends – include in Main Document, include notes for any abbreviations

Figures – for **initial peer review**, any format is fine, and they can be included in the Main Document

For **revisions**, these should be submitted individually either in the program of origin or as TIF, PNG, or EPS files with at least 300 pixels/inch resolution. Make sure there is a legend and axis labels. They should NOT have 3D, shadows, color, or other graphic enhancements. Do not include the title or notes in the images.