

## **Epinephrine Use in Out-of-Hospital Cardiac Arrest**

**Clinical Bottom Line:** The use of epinephrine in out-of-hospital cardiac arrests increased the chance for ROSC and improved 30 day mortality, however we are concerned about the increase in severe neurological outcomes. If all of the extra survivors are neurologically devastated, we do not feel epinephrine should be routinely used. Given that this has been the standard in out-of-hospital cardiac arrest for many years, though, we feel more studies are needed before clinicians will be comfortable withholding this treatment.

### **PICO Question:**

**P:** Patients with out of hospital cardiac arrest

**I:** Epinephrine 1 mg every 3-5 minutes

**C:** Normal Saline Injection

**O:** 30 day mortality and hospital discharge; secondary outcomes measuring neurological status

**Background:** In outside hospital cardiac arrest the use of epinephrine has played a key role in ACLS in the United States for over 60 years. Epinephrine works as a alpha antagonist which causes vasoconstriction and works to increase aortic diastolic pressure during CPR. Studies have been performed in the past which reveal that epinephrine improves ROSC as well as short term survival. However, recent studies have been exploring both the long term survival rate of epinephrine as well as neurological effects that epinephrine has on those who have long term survival. In these two studies both standard of care, epinephrine 1mg, is compared to placebo, normal saline, in order to evaluate survival and neurologic outcomes in those individuals who undergo outside hospital cardiac arrest.

### **Trial 1**

Perkins, et al. "A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest." *The New England Journal of Medicine*. July 18, 2018.

[https://www.nejm.org/doi/full/10.1056/NEJMoa1806842?query=recirc\\_mostViewed\\_railB\\_article](https://www.nejm.org/doi/full/10.1056/NEJMoa1806842?query=recirc_mostViewed_railB_article)

**Validity Rating:** Low Risk of Bias

**The Basics:** Multicenter, randomized, double-blind, placebo controlled trial which studied 8014 patients with out of hospital cardiac arrest. Patients randomized into 2 treatment groups (listed below). Excluded from these groups were those who achieved ROSC prior to administration of epinephrine by trial-trained response team.

1. Epinephrine 1 mg every 3-5 minutes
2. Saline Injection

**Exclusion Criteria:** Patients < 16 years old, known or suspected pregnancy, cardiac arrest from anaphylaxis or asthma, administration of epinephrine prior to arrival of trial-trained paramedics. Traumatic cardiac arrests excluded in one ambulance.

**Primary Outcome:** 30 day survival

**Secondary Outcomes:** Neurological outcomes at hospital discharge and at 3 months (mRS  $\leq$  3), rate of survival until hospital admission, lengths of stay in hospital and ICU, rates of survival at hospital discharge and at 3 months.

**Follow Up:** < 10% lost to follow up before primary outcome analysis. Main follow up categories consisted of survival analysis (30d and 3 months) and neurologic analysis (status at hospital discharge and 3 months).

**Results:**

1. Improved 30 day survival in epinephrine group: 3.2% v 2.4% (OR 1.39, 95% CI 1.06-1.82,  $p < 0.02$ )
  - a. Epi group had improved chances of ROSC (36.3% v 11.7%)
  - b. NNT to prevent 1 death after cardiac arrest was 112
2. No statistical difference in favorable neurological survival (mRS of 3 or less) at hospital discharge or at 3 months 2.1% v 1.6% (OR 1.31, 95% CI 0.94-1.82).
  - a. Increased severe neurological outcomes in survivors of epinephrine group.

**Limitations and Bias:**

1. No data on baseline neurological status
2. No data on underlying disease that could affect prognostic outcomes
3. Hospital based care was not specified in the trial protocol (though it did follow national guidelines)
4. The original protocol anticipated a higher survival rate than the one that was observed.

## Trial 2

Jacobs et. al "Effect of adrenaline on survival in out-of-hospital cardiac arrest: A randomised double-blind placebo-controlled trial." Resuscitation. September 2011.

<https://www.sciencedirect.com/science/article/pii/S0300957211004059>

**Validity Rating:** Low Risk of Bias

**The Basics:** Double blind randomised placebo controlled trial conducted in Western Australia in which there were 4103 cardiac arrests were attended by ambulance, however 601 patients were randomised in to the two groups:

UAMS Journal Club Summary  
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Drs Pampolina and Ruby  
Faculty Advisor: Dr. Carly Eastin

1. Epinephrine 1 mg every 3-5 minutes
2. 0.9% NS every 3-5 minutes

**Exclusion Criteria:** <16 years of age

**Primary Outcome:** Survival to hospital discharge

**Secondary Outcome:** Prehospital ROSC, survival to admission, and Cerebral Performance Category score at time of hospital discharge

**Follow Up:** 0% were lost to follow up

**Results:** When concerning the primary endpoint there was no significant difference in normal saline vs epinephrine when administered to patients in cardiac arrest outside of the hospital; odds ratio 2.2 (95% CI 0.7-6.3). Epinephrine did show improved survival in both obtaining ROSC prior to the hospital, 23.5% vs 8.4% with an odds ratio of 3.4 (95% CI 2-5.6) as well as being admitted to the hospital 13% vs 25.4% with an odds ratio of 2.3 (95% CI 1.4-3.6). There was also no statistical difference in the cerebral performance category score at time of hospital discharge; odds ratio unable to be calculated.

**Limitations and Biases:**

1. Small number of patients that obtained ROSC outside hospital in order to obtain complete statistical data
2. Unable to assess the influence of CPR quality and timing of epinephrine administration
3. Unable to exclude selection bias
4. Baseline neurologic status of patients that had cardiac arrest