Is Epinephrine During Cardiac Arrest Associated With Worse Outcomes in Resuscitated Patients?

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Disclosures

Abstract and Introduction

Methods We included all patients with OHCA who achieved successful ROSC admitted to a cardiac arrest center from January 2000 to August 2012. Use of epinephrine was coded as yes/no and by dose (none, 1 mg, 2 to 5 mg, >5 mg). A favorable discharge outcome was coded using a Cerebral Performance Category 1 or 2. Analyses incorporated multivariable logistic regression, propensity scoring, and matching methods.

Results Of the 1,556 eligible patients, 1,134 (73%) received epinephrine; 194 (17%) of these patients had a good outcome versus 255 of 422 patients (63%) in the nontreated group (p < 0.001). This adverse association of epinephrine was observed regardless of length of resuscitation or in-hospital interventions performed. Compared with patients who did not receive epinephrine, the adjusted odds ratio of intact survival was 0.48 (95% confidence interval [CI]: 0.27 to 0.84) for 1 mg of epinephrine, 0.30 (95% CI: 0.20 to 0.47) for 2 to 5 mg of epinephrine, and 0.23 (95% CI: 0.14 to 0.37) for >5 mg of epinephrine.
Delayed administration of epinephrine was associated with worse outcome.

**Conclusions** In this large cohort of patients who achieved ROSC, pre-hospital use of epinephrine was consistently associated with a lower chance of survival, an association that showed a dose effect and persisted despite post-resuscitation interventions. These findings suggest that additional studies to determine if and how epinephrine may provide long-term functional survival benefit are needed.

**Introduction**

International resuscitation guidelines recommend administering epinephrine every 3 to 5 min during cardiac arrest resuscitation regardless of the initial rhythm.\[1\] The alpha-adrenergic effects of epinephrine can increase coronary and cerebral perfusion pressure during the resuscitation period\[2,3\] and subsequently help achieve return of spontaneous circulation (ROSC). However, epinephrine may exert adverse effects during the post-resuscitation phase and contribute to myocardial dysfunction, increased oxygen requirements, and microcirculatory abnormalities\[4–8\]. Although epinephrine can increase the likelihood of achieving ROSC, the balance of the effects of epinephrine on long-term survival remains uncertain. A randomized study found no overall survival effect of medication treatments that included epinephrine.\[9\] In a large observational study, epinephrine was associated with a lower likelihood of long-term survival.\[10\] In each of these studies, epinephrine was associated with a greater likelihood of ROSC, but the early potential benefit did not translate into a greater likelihood of long-term survival because outcomes among the epinephrine-treated patients were worse during the post-resuscitation phase.

We sought to better understand the potential adverse effects of epinephrine when used during the post-resuscitation phase. We evaluated the relationship between use of epinephrine during resuscitation and survival among a cohort of patients resuscitated from out-of-hospital cardiac arrest (OHCA) and admitted to the hospital with ROSC. We also evaluated whether evidence-based post-resuscitation interventions, such as coronary reperfusion or hypothermia, may influence this epinephrine-survival relationship.