
Comparison of IV Epinephrine and IV Norepinephrine in Cardiac Arrest Patients with Return of Spontaneous Circulation

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Abstract

Introduction

Out-of-hospital cardiac arrest (OHCA) affects approximately 350,000 individuals annually in the United States, with a low survival rate of around 9.1%.¹ Post-resuscitation shock following return of spontaneous circulation (ROSC) is a common occurrence, characterized by vasoplegia, myocardial dysfunction, and hypovolemia. Epinephrine, the historically preferred vasopressor, may worsen myocardial oxygen demand and increase arrhythmia risk.² Norepinephrine, which has stronger alpha-adrenergic activity and fewer beta-adrenergic effects, may offer improved outcomes with fewer complications.³

Methods

A retrospective chart review was conducted at Dignity Health campuses between January 1, 2021 and December 31, 2024. Patients ≥ 18 years old who achieved ROSC after OHCA or ED cardiac arrest and received either IV epinephrine or IV norepinephrine were included. Exclusions were DNR orders within 24 hours, incomplete documentation, or receipt of both agents within 30 minutes post-ROSC. The primary outcome was recurrent cardiac arrest. Secondary outcomes included survival to admission, discharge, use of ≥ 3 vasopressors, vasopressin use, and tachycardic arrhythmias.

Results

A total of 84 patients met inclusion criteria (n=61 norepinephrine, n=23 epinephrine) of the 771 patient profiles that were reviewed. Baseline characteristics were similar between groups, including mean age (~72 years), sex distribution, and initial non-shockable rhythm. Recurrent cardiac arrest occurred in 11.5% of norepinephrine patients and 26.1% of epinephrine patients (OR 0.4, 95% CI 0.11-1.43; p=0.156). Survival to admission trended higher in the norepinephrine group (52.5% vs 30.4%; OR 2.54, 95% CI 0.9-7.21; p=0.08), as did survival to discharge (9.8% vs 4.4%; OR 2.18, 95% CI 0.23-20.33; p=0.493). Use of vasopressin and additional vasopressors was comparable between groups.

Conclusion

IV norepinephrine was associated with a trend toward lower recurrent cardiac arrest and improved survival metrics compared to IV epinephrine in ROSC patients. While not statistically significant, these findings support further investigation into norepinephrine's role in post-cardiac arrest care.

Keywords: Cardiac arrest, return of spontaneous circulation, vasopressors, norepinephrine, epinephrine, post-resuscitation shock

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Introduction

Out-of-hospital cardiac arrest (OHCA) continues to present a significant public health burden, with over 350,000 events annually in the U.S. and survival rates below 10%.¹ While successful resuscitation results in return of spontaneous circulation (ROSC), patients often enter a critical state known as post-resuscitation shock. This condition involves systemic inflammation and ischemia-reperfusion injury that results in vasodilation, capillary leak, and myocardial dysfunction.^{2,3}

Historically, epinephrine has been the standard vasopressor for initial cardiac arrest management due to its strong alpha adrenergic and beta adrenergic stimulation, which increases heart rate and cardiac output. However, the same properties that make epinephrine effective during arrest may be detrimental post-ROSC by increasing myocardial oxygen demand and precipitating arrhythmias.²

Norepinephrine, which exerts potent alpha-adrenergic vasoconstriction with limited beta stimulation, is often preferred in septic shock due to its ability to maintain perfusion pressure without excessive tachycardia. Its utility in post-ROSC care is not well defined but may offer a hemodynamic profile more conducive to maintaining organ perfusion without exacerbating myocardial stress.³

This study compares IV norepinephrine and IV epinephrine in patients who achieved ROSC after OHCA or in-hospital arrest. Outcomes evaluated include recurrent cardiac arrest and survival metrics.

Methods

This study was a retrospective chart review conducted at Dignity Health St. Rose Dominican Hospital campuses, including Siena, San Martin, and Rose de Lima. Data were collected from January 1, 2021, through December 31, 2024. Patients eligible for inclusion were aged 18 years or older who had experienced OHCA or cardiac arrest in the emergency department and achieved ROSC. To be included, patients must have received either IV epinephrine or IV norepinephrine as vasopressor support following ROSC. Patients were excluded if they had documented do-not-resuscitate (DNR) orders within 24 hours of the event, if there was incomplete documentation regarding vasopressor use, or if both vasopressors were administered within 30 minutes post-ROSC.

The primary outcome assessed was the incidence of recurrent cardiac arrest following ROSC. Secondary outcomes included survival to hospital admission, survival to hospital discharge, use of three or more additional vasopressors, use of vasopressin, and incidence of tachycardic arrhythmias.

Statistical Analysis

Statistical analyses included Fisher's exact test for categorical variables and two-sample t-tests for continuous variables. Logistic regression was used to control for age and sex. Based on power calculations, a total of 346 patients were needed to detect a 15% absolute risk reduction with 80% power and an alpha of 0.05.

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Table 1: Baseline characteristics

Baseline Characteristics	IV Norepinephrine (n = 61)	IV Epinephrine (n = 23)	P-value
Age, yr. (mean $\pm$ SD)	72.48 $\pm$ 12	72.39 $\pm$ 11	0.977
Female, No. (%)	22 (36.1)	12 (52.2)	0.217
Out-of-hospital cardiac arrest, No. (%)	53 (86.9)	21 (91.3)	0.72
Initial rhythm being non-shockable, No. (%)	56 (91.8)	22 (95.6)	1

Results

Of the total of 771 patient profiles reviewed, a total of 84 patients met inclusion criteria, with 61 patients receiving IV norepinephrine and 23 patients receiving IV epinephrine. Baseline demographics were similar between groups. The mean age was 72.48 years ($\pm$ 12) in the norepinephrine group and 72.39 years ($\pm$ 11) in the epinephrine group ($p=0.977$). Females comprised 36.1% of the norepinephrine group and 52.2% of the epinephrine group ($p=0.217$). Most patients had experienced OHCA (86.9% in the norepinephrine group and 91.3% in the epinephrine group; $p=0.72$), and a non-shockable rhythm was the initial rhythm in 91.8% and 95.6% of patients, respectively.

For the primary outcome, recurrent cardiac arrest occurred in 7 patients (11.5%) in the norepinephrine group compared to 6 patients (26.1%) in the epinephrine group. This difference was not statistically significant (OR 0.4; 95% CI 0.11–1.43; $p=0.156$).

Regarding secondary outcomes, survival to hospital admission was 52.5% in the norepinephrine group compared to 30.4% in the epinephrine group (OR 2.54; 95% CI 0.9–7.21; $p=0.08$). Survival to hospital discharge

occurred in 6 patients (9.8%) in the norepinephrine group versus 1 patient (4.4%) in the epinephrine group (OR 2.18; 95% CI 0.23–20.33; $p=0.493$). Seven patients (11.5%) in the norepinephrine group required three or more vasopressors, compared to four patients (17.4%) in the epinephrine group ($p=0.511$). Use of vasopressin was reported in 20 patients (32.8%) in the norepinephrine group versus 4 patients (17.4%) in the epinephrine group (OR 2.68; 95% CI 0.78–9.23; $p=0.132$).

Table 2: Primary Outcomes

	IV Norepinephrine (n = 61)	IV Epinephrine (n = 23)	OR (95% CI)	P-value
Recurrent cardiac arrest, No. (%)	7 (11.5)	6 (26.1)	0.4 (0.11 - 1.43)	0.156

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Table 3: Secondary Outcomes

	IV Norepinephrine (n = 61)	IV Epinephrine (n = 23)	OR	P-value
Survival rate to admission	32 (52.5)	7 (30.4)	2.54 (0.9 - 7.21)	0.08
Survival rate to discharge	6 (9.8)	1 (4.4)	2.18 (0.23 - 20.33)	0.493
Additional use of ≥ 3 other vasopressors	7 (11.5)	4 (17.4)	0.64 (0.16 - 2.47)	0.511
Use of vasopressin	20 (32.8)	4 (17.4)	2.68 (0.78 - 9.23)	0.132

Discussion

In this retrospective review, norepinephrine was associated with a lower incidence of recurrent cardiac arrest and higher survival rates to hospital admission and discharge compared to epinephrine, although these findings did not reach statistical significance. The trend observed may be clinically meaningful and aligns with known pharmacological differences between the two agents. Epinephrine's beta-adrenergic activity can increase myocardial oxygen consumption, potentially contributing to arrhythmogenesis and myocardial dysfunction, especially in the vulnerable post-ROSC phase.² In contrast, norepinephrine's more selective alpha-adrenergic effect may support vascular tone and perfusion without the same degree of chronotropy or myocardial oxygen demand.³

While the study did not demonstrate significant differences in outcomes, the directionality of effect sizes, especially for recurrent arrest and survival to admission, favors norepinephrine and warrants further exploration. Additionally, although not statistically significant, the higher use of vasopressin in the norepinephrine group may reflect greater hemodynamic support efforts or institutional practice variability. The study was limited by a relatively small sample size, single health system setting, and retrospective design. The reliance on documentation quality and coding accuracy further constraints interpretability.

Moreover, the study was underpowered to detect modest differences between groups, and confounding variables may not have been fully controlled despite statistical adjustments.

Conclusion

Although not statistically significant, this study found that IV norepinephrine was associated with lower rates of recurrent cardiac arrest and a trend toward improved survival outcomes when compared to IV epinephrine in post-ROSC patients. These results suggest potential clinical benefits of norepinephrine as a first-line vasopressor in the immediate post-resuscitation setting. Given the limitations of retrospective analyses, prospective randomized controlled trials are necessary to confirm these findings and guide clinical practice.

Conflicts of Interest

The author has no conflicts of interest to declare.

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