

Epinephrine for Cardiac Arrest: The Neurological Paradox

It reliably restores a pulse. It has never been proven to save the brain, and may harm it.

↑ ROSC

Epinephrine strongly increases return of spontaneous circulation (RR ~3.1)

→ Brain

No RCT shows improved neurologically intact survival

31% vs 18%

Severe neuro impairment (mRS 4-5) among PARAMEDIC2 survivors, epi vs placebo

Why it helps the heart

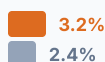
- Alpha-1 vasoconstriction raises aortic diastolic and coronary perfusion pressure (CPP).
- Higher CPP drives ROSC. Reliable, immediate pressor.

Why it may harm the brain

- Cerebral vasoconstriction reduces brain flow during CPR.
- Post-ROSC capillary no-reflow (imaged); blood-brain barrier disruption.

The paradox in the numbers (PARAMEDIC2, N=8,014)

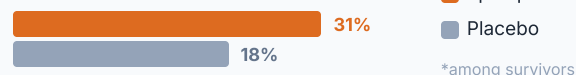
30-day survival



Favorable neuro



Severe impairment*



Evidence at a glance

Study	Design / N	Key outcome
PARAMEDIC2 2018	RCT, N=8,014	30-day survival 3.2% vs 2.4% (OR 1.39); neuro NS; severe impairment 31% vs 18% of survivors
Jacobs 2011	DBRCT, N=534	ROSC 23.5% vs 8.4%; survival not significant
Olasveengen 2009	RCT, N=851	IV drugs vs no IV access: short-term ROSC up; survival and neuro not significant
Gueugniaud 1998	RCT, N=3,327	High-dose vs standard epinephrine: more ROSC, no survival or neuro benefit
Hagihara 2012	Obs, N=417,188	ROSC up (aOR 2.51); 1-mo survival down (aOR 0.54); good neuro down (aOR 0.21)
Aves 2020	Meta, 17 RCTs	ROSC RR 3.09; survival RR 1.44; no neuro benefit
Jaeger 2022	Registry	Higher cumulative dose → worse neuro (a signal, not a ceiling)
Fukuda 2021	Cohort, N=119,946	Each 1-min delay to epinephrine: aOR 0.91 for good neuro; earlier is better
Oghifobibi 2022	Preclinical, imaging	Direct visualization of epinephrine-induced cerebral capillary no-reflow post-ROSC

Dose & timing (2025 AHA): epinephrine 1 mg IV/IO q3-5 min (Class IIa, B-R); IV preferred. Non-shockable: as soon as feasible. Shockable: after initial defibrillation attempts fail.

Bottom line: do not withhold epinephrine, standard of care. Give it early per rhythm; do not cap on total dose. Compressions and early defibrillation come first.

For educational purposes only. A continuing-education aid for pharmacists and health professionals. Not medical advice, not a substitute for clinical judgment or the complete AHA guidelines. Verify doses against current primary sources.