

Citation: Andersen LW, et al., [Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest: A Randomized Clinical Trial](#). JAMA. 2021 Oct 26;326(16):1586-1594.

Methodology (Study design): This was a multicenter randomized controlled trial in 10 hospitals in Denmark on approximately 500 adult patients with cardiopulmonary arrest. The study groups were (1) a control group, in which the standard ACLS protocol was followed and paired with administration of epinephrine and saline, and (2) an intervention group, in which the standard ACLS protocol was followed and paired with administration of epinephrine, vasopressin, and steroids. In the intervention group, each dose of epinephrine was immediately followed by 40 mg of methylprednisolone and 20 units of vasopressin for up to 4 rounds of CPR. The primary outcome was ROSC achievement. The secondary outcomes were any effects on favorable neurologic outcomes at 30 days. The general patient population was 64% men with an average age of 71 years. Approximately 90% of patients presented with an initial nonshockable rhythm (predominantly pulseless electrical activity). In both groups, the first dose of medications was attempted to be administered in the first 5-8 minutes. The primary outcome was return of spontaneous circulation. Secondary outcomes included survival and favorable neurologic outcome at 30 days (Cerebral Performance Category score of 1 or 2).

Strengths: It is a large randomized control trial. The randomization was good, and the groups were balanced. Most in-hospital arrests occurred in medical and medical-surgical units. The trial was double-blind, with patients, investigators, clinicians, and outcome assessors unaware of the allocated treatment.

Weaknesses: lack of generalizability (many reasons for excluding a patient). lack of consistent early administration. (The authors noted that although most patients received an initial dose of medications within 8 minutes, some instances of late delivery occurred). "outcomes in Denmark may be more favorable than those in other countries."

My Clinical Bottom Line:

The theories:

- vasopressin can cause vasoconstriction, thus increasing arterial blood pressure and coronary perfusion pressure, which together may improve the chances of obtaining return of spontaneous circulation (ROSC).
- steroids increase cortisol levels, which may also increase the chances of achieving ROSC.

In the intervention group, approximately 42% of patients achieved ROSC, compared with 33% in the control group. (risk ratio, 1.30 [95% CI, 1.03-1.63]; risk difference, 9.6% [95% CI, 1.1%-18.0%]; P = .03). In the subgroup analysis, the main features of the patients in the intervention group included an initial shockable rhythm, younger age, witnessed arrest, and early administration of ACLS medications.

At 30 days, 23 patients (9.7%) in the intervention group and 31 patients (12%) in the placebo group were alive (risk ratio, 0.83 [95% CI, 0.50-1.37]; risk difference: -2.0% [95% CI, -7.5% to 3.5%]; P = .48). A favorable neurologic outcome was observed in 18 patients (7.6%) in the intervention group and 20 patients (7.6%) in the placebo group at 30 days (risk ratio, 1.00 [95% CI, 0.55-1.83]; risk difference, 0.0% [95% CI, -4.7% to 4.9%]; P > .99).

The results showed a higher percentage of ROSC in patients who received adjunct medications. However, for most of us, the endpoint that matters is neurologically meaningful survival, which these medications do not change.

Overall, this study establishes that these adjuncts paired with the standard ACLS algorithm are more likely to lead to ROSC but may not necessarily improve functional patient outcomes.