Critical Review Form
Therapy

Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. N Engl J Med. 2002 Mar 21;346(12):884-90.

Objectives: **"The Amiodarone versus Lidocaine in Prehospital Ventricular Fibrillation Evaluation (ALIVE) was a double-blind, controlled clinical trial comparing amiodarone with lidocaine in patients with out-of-hospital ventricular fibrillation in Toronto." (p. 884)**

Methods: **This randomized controlled trial was conducted in the Toronto Emergency Medical Services system, a multi-centered emergency-response system serving 17 community hospitals, between November 1995 and April 2001. Kits were placed on ambulances using block randomization with blocks of four. Kits contained either active amiodarone and lidocaine placebo or active lidocaine and amiodarone placebo. When given, amiodarone (5 mg/kg estimated body weight), or its matching placebo, and lidocaine (1.5 mg/kg), or its matching placebo, were rapidly administered by peripheral IV, along with further shocks as necessary and further ACLS. If ventricular fibrillation persisted after a further shock, a second dose of study drug (lidocaine 1.5 mg/kg or amiodarone 2.5 mg/kg) were given along with matching placebo as attempts at further resuscitation were continued.**

The primary outcome was survival to admission to the ICU. Secondary outcomes were survival to hospital discharge and adverse events, defined as the need to administer atropine or dopamine following study drug administration.

During the study period, 347 patients were randomly assigned to receive either amiodarone (n = 180) or lidocaine (n = 167). The mean ages were 68 and 66 years, respectively, and 76% and 81% were male. The rhythm at the time of drug administration was ventricular fibrillation in 91% and 93% of cases and ventricular tachycardia in 2% of cases in each group. Eighty-seven patients in the amiodarone group and 86 patients in the lidocaine group received a second dose of the study drug.

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Guide	Comments
Are the results valid?	
Did experimental and control groups being the study with a similar prognosis?	
Were patients randomized?	Yes. Using block randomization with a block size of 4, kits containing either amiodarone or lidocaine with a matching placebo were placed on ambulances. The authors provide no information on how the randomization sequence was generated.

Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	Uncertain. There was no information on sequence generation, kit preparation, kit distribution, or how allocation concealment was maintained throughout this process.
Were patients analyzed in the groups to which they were randomized?	Presumably yes. While the authors do not specifically mention using an intention to treat analysis, it appears that only patients were received at least one dose of medication from the study kit were included in the analysis. The authors make no mention of inclusion of any patients who did not receive at least one dose of study medication.
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to gender, age, history of cardiac disease, witnessed arrest, bystander CPR, initial cardiac rhythm, rhythm at the time of drug administration, and time from dispatch to response or procedure.
Did experimental and control groups retain a similar prognosis after the study started?	
Were patients aware of group allocation?	No. Patients were in cardiac arrest at the time and all participants were blinded to group allocation with the use of study medication and matching placebo.
Were clinicians aware of group allocation?	No. See above.
Were outcome assessors aware of group allocation?	Likely yes, however the authors make no specific mention of blinding outcome assessors.
Was follow-up complete?	
What are the results?	
How large was the treatment effect?	• Patients in the amiodarone group were more likely to survive to hospital admission compared to the lidocaine group: 22.8% vs. 12.0%; OR 2.17, 95% CI 1.21 to 3.83. o Adjusted OR 2.49, 95% CI 1.28 to 4.85. • There were no differences between the treatment groups in the proportions of patients who needed treatment of bradycardia. • There was no statistically significant difference in survival to hospital discharge between the groups, with a trend toward improved outcomes in the amiodarone group: OR 1.69, 95% CI 0.56 to 5.16.
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	See above.
How can I apply the results to patient care?	
Were the study patients similar to my patient?	Mostly yes. This study was conducted in a large, urban EMS system in Toronto, where I expect patients and the medical care they receive to be similar to our community. While there are likely different in ethnic makeup and the proportion of patients with health insurance, I do not expect either of these to influence outcomes in out-of-hospital cardiac arrest.
Were all clinically important outcomes considered?	No. The primary outcome was short-term survival to hospital admission. While the authors did assess survival to hospital discharge, they did not assess neurologic outcome at discharge or more long-term functional outcomes. While some groups have recommended 90-day neurologic outcomes as a better measure in cardiac arrest (Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee) such outcomes are more difficult and more expensive to measure. The authors also do not report hospital length of stay, ICU length of stay, or cost.

Are the likely treatment benefits worth the potential harm and costs?	Unclear. While this study demonstrated improved survival to hospital admission with the use of amiodarone compared to lidocaine for refractory VF/VT, there was no statistically significant benefit for survival to hospital discharge. Additionally, the authors did not assess neurologic outcomes or more long-term outcomes.

Limitations:

1. **No information on sequence generation, kit preparation, kit distribution, or how allocation concealment was maintained throughout this process.**

2. **The primary outcome was short-term survival to hospital admission. While the authors did assess survival to hospital discharge, they did not assess neurologic outcome at discharge or more long-term functional outcomes.**

Bottom Line:

This randomized controlled trial demonstrated improved survival to hospital admission with the use of amiodarone compared to lidocaine for refractory VF/VT in out-of-hospital cardiac arrest, there was no statistically significant benefit for survival to hospital discharge. Additionally, the authors did not assess neurologic outcomes or more long-term outcomes.