The ALIVE Trial: Amiodarone Versus Lidocaine In Pre-Hospital Refractory Ventricular Fibrillation Evaluation

Based on preliminary data of Dorian P et al as presented at the 22nd Annual Scientific Sessions of the North American Society of Pacing and Electrophysiology; May 2–5, 2001; Boston.

Introduction

- The ALIVE (**A**miodarone versus **L**idocaine **I**n Pre-Hospital Cardiac Arrest Due to **V**entricular **F**ibrillation) study[2,3] was conducted by St. Michael's Hospital/University of Toronto and Toronto Emergency Medical System to compare amiodarone with lidocaine in patients with out-of-hospital cardiac arrest due to refractory VF.
- Treatment protocols for Advanced Cardiac Life Support (ACLS) have traditionally included epinephrine and lidocaine as primary pharmaceutical interventions for out-of-hospital ventricular fibrillation (VF).
- Despite the widespread acceptance of lidocaine as an anti-arrhythmic agent, few controlled studies have examined the effectiveness of lidocaine for the acute treatment (as opposed to prophylaxis) of malignant ventricular arrhythmias in the out-of-hospital setting.
- On the other hand, results of the ARREST trial[1] showed a significant benefit for intravenous (IV) amiodarone (versus placebo) in improving survival to hospital admission in cardiac arrest patients with shock-refractory VF.

Objective

- To determine whether amiodarone compared with lidocaine could improve survival rates to hospital admission in patients with shock-refractory, out-of-hospital cardiac arrest.

Methods

Study Design

- Prospective, randomized, controlled, blinded, double-dummy trial of IV amiodarone and IV lidocaine in patients with out-of-hospital cardiac arrest due to persistent or recurrent VF.

Patient Population

Inclusion Criteria

- Male or female patients who:
  - were treated by land paramedics during study period
  - were determined by treating paramedic(s) to be in documented VF
  - suffered persistent/recurrent VF despite three defibrillation shocks, epinephrine infusion (1.0 mg), and fourth shock
  - had IV access obtained during resuscitation

Exclusion Criteria

- Age <18 years.
- Cardiac arrest caused by noncardiac causes (poisoning, trauma, etc.).

Study Medication

Antiarrhythmic	Initial Doses	Supplemental Dose
IV amiodarone	5 mg/kg	2.5 mg/kg
IV lidocaine	1.5 mg/kg	1.5 mg/kg

Main Outcome Measures

Primary End Point

- Survival to hospital admission.

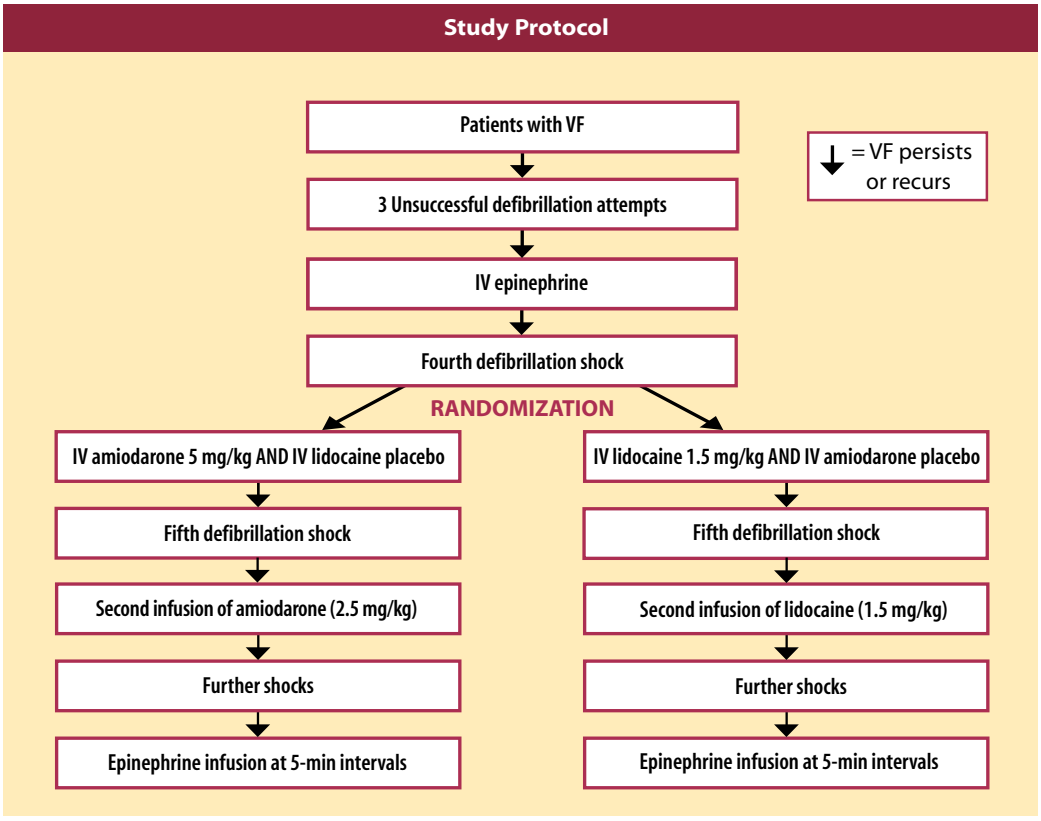
Secondary End Points

- Survival to hospital admission by initial rhythm (VF, pulseless electrical activity, asystole).
- Survival to hospital admission by time from EMS (Emergency Medical System) crew dispatch to study drug administration.
- Survival to hospital discharge.

Study Procedures

- Information abstracted from ambulance call reports, central dispatch log sheets, and hospital charts (for admitted patients).
- Patients surviving to hospital admission were followed for functional status at discharge as part of the study procedure; however, results are not yet available.

Figure 1



Data from Dorian et al.[3]

Statistical Analysis

- Two-sample comparison of proportions comparing the rates of primary end point in the two study groups.
- Overall type-I error set at 0.05.

Results

Table 1 **Demographics and Baseline Characteristics**

Characteristic	Amiodarone (n = 179)	Lidocaine (n = 165)	*P* Value
Age (yr)	68 ± 14*	66 ± 13*	NS
% Male	75	81	NS
Weight (kg)	80 ± 16*	82 ± 13*	NS
History of heart disease (%)	61.2	60.0	NS
Witnessed arrest (%)	76.4	79.3	NS
Bystander CPR (%)	26.4	28.7	NS
Initial rhythm (%):			
VF	78.5	80.5	NS
Asystole	10.7	9.8	NS
PEA	7.9	6.1	NS
Last recorded rhythm before study drug administration (%):			
VF	90.8	92.7	NS
VT	1.7	2.4	NS
Asystole	1.2	1.2	NS
PEA	4.6	3.1	NS
SV	1.7	0.6	NS
Total no. of shocks	5 ± 1.9*	5 ± 2.2*	NS

Abbreviations: CPR, cardiopulmonary resuscitation; NS, not significant; PEA, pulseless electrical activity; SD, standard deviation; SV, supraventricular; VF, ventricular fibrillation; VT, ventricular tachycardia.

*The values shown are means ± SD.

Data from Dorian et al.[3]

Survival to Hospital Admission

- More than twice as many patients survived to hospital admission in the group receiving IV amiodarone than in the group receiving IV lidocaine (22.7% vs. 11.0%).

	Amiodarone	Lidocaine	*P* Value
No. of patients surviving to hospital admission*	40 (22.7%)	18 (11.0%)	0.043
Odds Ratio: 2.37 (95% CI: 1.30, 4.33); *Relative Risk Reduction:* 52%			

*Intention-to-treat analysis

- Survival to hospital admission increased by 106% in patients receiving amiodarone versus patients receiving lidocaine (22.7% vs.11.0%).

Figure 2

Survival to Hospital Admission by Initial Rhythm

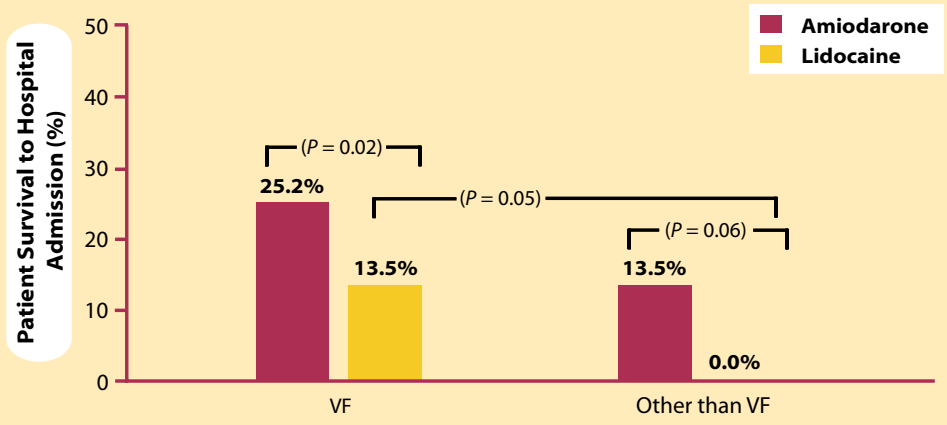
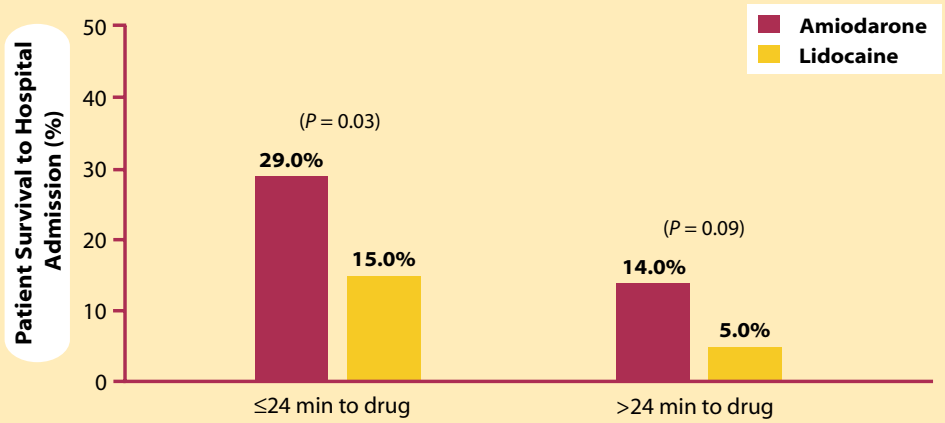


Table 2 **Time Intervals in Minutes From Emergency Crew Dispatch**

From Dispatch to:	Amiodarone (n = 179)	Lidocaine (n = 165)	*P* Value
Arrival at patient	7.3 ± 2.7	7.5 ± 2.6	NS
First defibrillation shock	11.8 ± 6.2	11.9 ± 6.9	NS
IV initiation	13.3 ± 4.3	13.6 ± 3.7	NS
Study drug	25.2 ± 8.0	24.1 ± 7.0	NS

Abbreviations: NS, not significant; SD, standard deviation.
The values shown are means ± SD.
Data from Dorian et al.[3]

Figure 3 **Survival to Hospital Admission by Lower and Upper Median of Time From Dispatch to Study Drug Administration (≤24 min vs. >24 min)***



*24 Minutes was determined to be the median time to administration of study drug for all patients.
Data from Dorian et al.[3]

Conclusions

- IV amiodarone is significantly (P = 0.043) more effective than lidocaine as an adjunct to ACLS procedures in patients with shock-resistant VF, with respect to patient survival to hospital admission.
- Survival rates by initial rhythm and by time from EMS crew dispatch to study drug administration were also significantly greater for patients receiving amiodarone.
- Rates of survival to hospital discharge are not yet available.

Clinical Significance

- The ALIVE trial provides evidence that suggests amiodarone is more effective than lidocaine in treating patients with acute VF in an out-of-hospital setting.

IV amiodarone is indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation and hemodynamically unstable ventricular tachycardia in patients refractory to other therapy.

IV amiodarone can also be used to treat patients with VT/VF for whom oral amiodarone is indicated, but who are unable to take oral medication.

IV amiodarone is contraindicated in patients with cardiogenic shock, marked sinus bradycardia, and second- or third-degree AV block in the absence of a functioning pacemaker.

IV amiodarone should be administered only by physicians who are experienced in the treatment of life-threatening arrhythmias, who are thoroughly familiar with the risks and benefits of amiodarone therapy, and who have access to facilities adequate for monitoring the effectiveness and side effects of treatment.

Hypotension is the most common adverse effect seen with IV amiodarone and may be related to the rate of infusion. Hypotension should be treated by slowing the infusion or with standard therapy: vasopressor drugs, positive inotropic agents, and volume expansion.

In clinical trials, the most important treatment-emergent adverse effects were hypotension (16%), bradycardia (4.9%), liver function test abnormalities (3.4%), cardiac arrest (2.9%), VT (2.4%), congestive heart failure (2.1%), cardiogenic shock (1.3%), and AV block (0.5%).

Please see Prescribing Information available at this display.

REFERENCES

1. Kudenchuk PJ, Cobb LA, Copass MK, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. *N Engl J. Med.* 1999;341:871-878.
2. Racht EM. Beyond "probable benefit": adding I.V. amiodarone to the EMS algorithm for cardiac arrest. *The Protocols Series.* 2001;3:3–13.
3. Dorian P, Cass D, Cooper R, et al. ALIVE: amiodarone versus lidocaine in pre-hospital refractory ventricular fibrillation evaluation. Presented at the 22nd Annual Scientific Sessions of the North American Society of Pacing and Electrophysiology; May 2–5, 2001; Boston.