The ARREST Trial: Amiodarone for Resuscitation After Out-of-Hospital Cardiac Arrest Due to Ventricular Fibrillation

Introduction

- The ARREST (**A**miodarone in out-of-hospital **R**esuscitation of **RE**fractory **S**ustained ventricular **T**achyarrhythmias) study was a prospective, randomized, double-blind, placebo-controlled study of intravenous amiodarone in patients with out-of-hospital cardiac arrest.[1] The study was designed to determine whether IV amiodarone could improve the rate of successful resuscitation in these patients.
- The results of the ARREST trial demonstrated for the first time that an antiarrhythmic agent, IV amiodarone, improved survival to hospital admission in patients with cardiac arrest due to persistent ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT).

- Intravenous amiodarone significantly and independently improved the rate of survival to hospital admission. Patients who received amiodarone for cardiac arrest due to VF/VT survived to hospital admission more often than patients who received placebo (44% vs. 34%; P = 0.03).

Objectives

- ARREST was designed to determine if the early use of intravenous amiodarone in patients with out-of-hospital cardiac arrest due shock-refractory VF or VT would increase the proportion of patients who survive the episode to be admitted to the hospital.
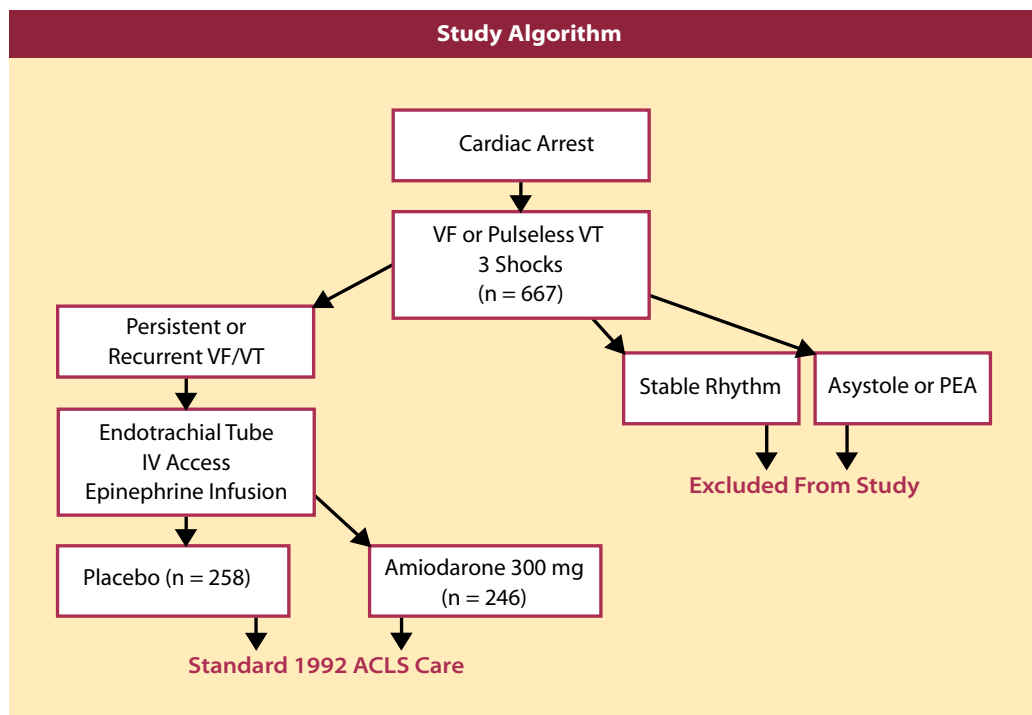
Patient Eligibility Criteria

- Older than 18 years of age

- Nontraumatic out-of-hospital cardiac arrest

- Ongoing or recurrent VF/VT after three or more cardioversion attempts (shocks)

- Medics on-scene (for study drug patients)

- IV access

Study End Points

- *Primary end point:* Admission to hospital with a spontaneously perfusing rhythm **(Figure 1)** meant that the patient had a sufficiently stable, organized rhythm and blood pressure (with or without the use of pressor drugs) to be assigned to a hospital bed.

Figure 1 — Study Algorithm

Cardiac Arrest

VF or Pulseless VT
3 Shocks
(n = 667)

Persistent or Recurrent VF/VT

Stable Rhythm

Asystole or PEA

Excluded From Study

Endotrachial Tube
IV Access
Epinephrine Infusion

Placebo (n = 258)

Amiodarone 300 mg
(n = 246)

Standard 1992 ACLS Care

Data from Kudenchuk et al.[1]

- Patients were stratified according to initial cardiac arrest rhythm **(Table 1)**:

    - VF

    - asystole

    - pulseless electrical activity (PEA)

Table 1	Patient Characteristics Before Study Drug Administration	
Characteristic	**IV Amiodarone** **(n = 246)**	**Placebo** **(n = 258)**
Male	76%	79%
Age (yr)	66 ± 14*	65 ± 14*
Cardiac history	64%	59%
Other medical history	47%	52%
VF amplitude (mV)	0.42 ± 0.2*	0.45 ± 0.2*
Witnessed arrest	70%	77%
Bystander CPR	68%	59%
Initial cardiac arrest rhythm:		
VF	83%	83%
Pulseless VT	0	0.4%
Asystole converting to VF	4%	5%
PEA converting to VF	12%	11%

*Values shown are the means ± SD.
Data from Kudenchuk et al.[1]

- *Secondary end points* **(Table 2)**:

    - Adverse effects

    - Number of shocks after administration of study drug

    - Total duration of resuscitation efforts

    - Need for additional antiarrhythmic drugs

- Survival to discharge from the hospital and functional neurological status at discharge were also evaluated, although, by design, the trial did not have sufficient power to demonstrate differences in these outcomes.

Table 2	Secondary End Point Results		
	IV Amiodarone	**Placebo**	***P* Value**
No. of shocks after study drug	4 ± 3*	6 ± 5*	0.17
Total duration of resuscitation efforts after study drug (min)	42 ± 16*	43 ± 16*	0.87
Treatment after study drug:			
Antiarrhythmics	80%	82%	0.70
Pressor agents (for survivors)	59%	48%	0.04
Bradycardia therapy (atropine)	41%	25%	0.004

*Values shown are means ± SD.
Data from Kudenchuk et al.[1]

- In the amiodarone group when compared with the placebo group, overall there were 29% more successful resuscitations, 26% more successful resuscitations among those whose initial rhythm was VF, and 56% more successful resuscitations among those patients in whom electrical defibrillation had produced a transient return of circulation **(Figure 2)**.


Figure 2 — Survival to Admission
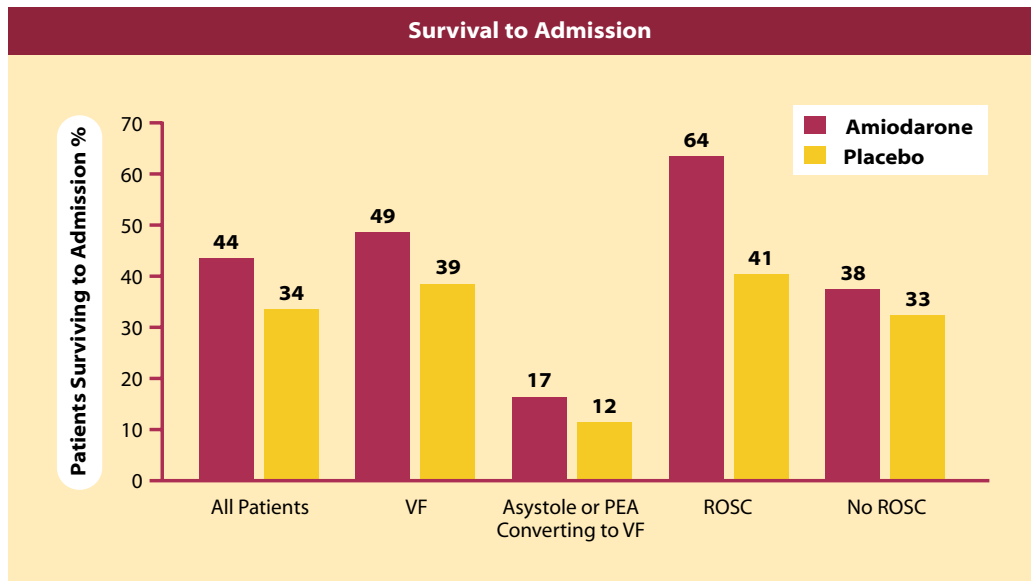
- The study was not sufficiently powered to detect an effect on survival to hospital discharge.

- The time of response (length of time to the administration of either amiodarone or placebo) had a sizable impact on survival to the hospital (Figure 3). However, the amiodarone group had a better outcome at all measured intervals, compared with the placebo group, and the benefit was consistent whether the drug was administered early or late ($P = 0.008$).

Figure 3
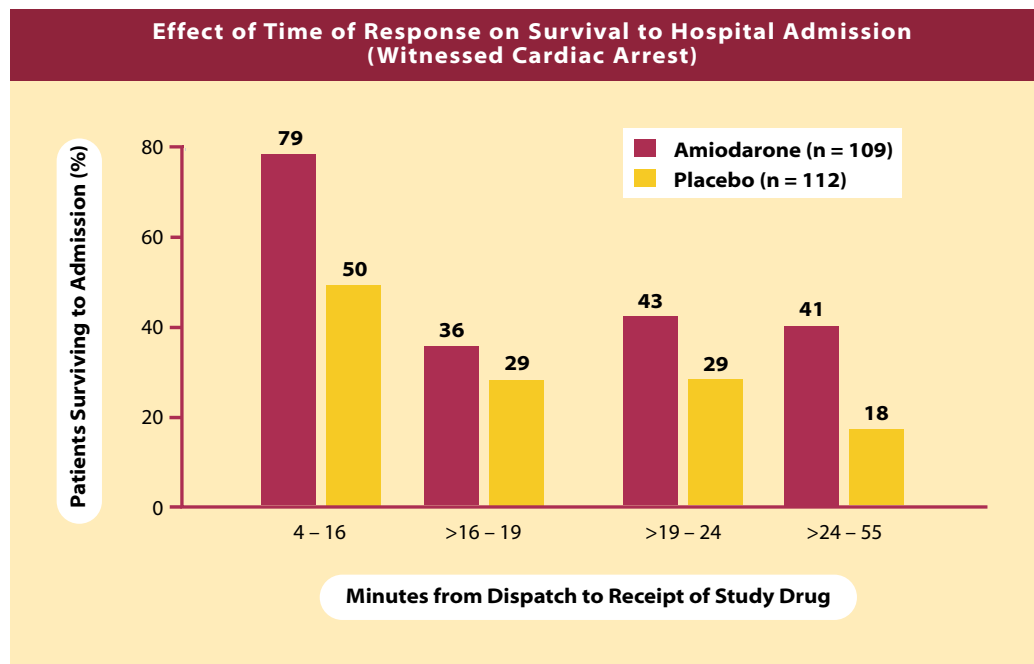
Effect of Time of Response on Survival to Hospital Admission (Witnessed Cardiac Arrest)

Other Predictors of Admission to Hospital

- There were other independent predictors of outcome (initial rhythm, presence or absence of ROSC, gender, etc.) in the ARREST trial in addition to the administration of amiodarone versus placebo (Tables 3 and 4). After adjustment for these factors, the odds ratio for survival in recipients of amiodarone versus recipients of placebo remained almost the same as before the adjustment (odds ratio 1.6, $P = 0.02$ after adjustment; odds ratio 1.5, $P = 0.03$ before adjustment).

Table 3	Characteristics of Resuscitation and Treatment Before Assignment to Amiodarone or Placebo		
Characteristic	**Amiodarone (n = 246)**	**Placebo (n = 258)**	***P* Value**
Transient ROSC	55 (22%)	52 (20%)	0.61
No. of shocks (mean ± SD)	5 ± 2	5 ± 2	0.73
Treatment for bradycardia	32 (13%)	51 (20%)	0.04
Pressor treatment	19 (8%)	22 (9%)	0.74
Antiarrhythmic drug treatment	65 (26%)	91 (35%)	0.04

Data from Kudenchuk et al.[1]

Table 4	Subgroup Analyses
Patient Characteristic	**% Survival to Hospital**

Initial Rhythm
  VF
  Asystole, PEA
	
	44
	14 ($P < 0.001$)

ROSC	53
No ROSC	30 ($P < 0.001$)
Female	43
Male	38 ($P = 0.06$)

Data from Kudenchuk et al.[1]

- More than half of the 67 patients discharged alive resumed independent living activities or returned to their former employment (55% in the amiodarone group, 50% in the placebo group).

Conclusions

- The use of IV amiodarone significantly improved survival to hospital admission for patients with cardiac arrest due to persistent VF/pulseless VT.

- The ARREST trial is the first controlled, randomized trial to show a benefit for using an antiarrhythmic agent in resuscitation attempts versus administering placebo.

- The ARREST trial provided solid evidence to support the inclusion of IV amiodarone in the 2000 ACLS guidelines.[2]

- Amiodarone administered before lidocaine, in addition to standard 1992 ACLS measures, resulted in the resuscitation of 29% more patients than did standard 1992 ACLS measures alone.

- The ARREST trial also underscores the importance of early defibrillation in improving survival in patients with cardiac arrest.

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. American Heart Association. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiac Care. *Circulation*. 2000;102(suppl):I–86—I–165.