**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care**

**Worksheet author(s)**

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| Ong, Marcus Eng Hock<br>Tommaso Pellis<br>Mark S Link | **Date Submitted for review:**<br>**Feb 4, 2010** |

**Clinical question.**

"In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of antiarrhythmic drugs (lidocaine, procainamide, amiodarone, bretylium, magnesium) or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O)."

**Is this question addressing an intervention/therapy, prognosis or diagnosis? intervention/therapy**
**State if this is a proposed new topic or revision of existing worksheet**: revision

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

**Search strategy (including electronic databases searched).**

Dr Ong's search strategy
PubMed "heart arrest" or "cardiopulmonary resuscitation" or "cardiac arrest" as MESH (headings) AND "Anti-Arrhythmia Agents" or "Lidocaine" or "Lignocaine" or "procainamide" or "amiodarone" or "bretylium" or "magnesium" as textword in headings or abstract
EMBASE search using text words (all fields) "Anti-Arrhythmia Agents" or "Lidocaine" or "Lignocaine" or "procainamide" or "amiodarone" or "bretylium" or "magnesium"AND (cardiac arrest OR resuscitation)
AHA EndNote Master library, Cochrane database for systematic reviews , Central Register of Controlled Trials, "Anti-Arrhythmia Agents", "Lidocaine", "Lignocaine", "procainamide", "amiodarone", "bretylium", "magnesium"
Review of references from articles. Forward search using SCOPUS and Google scholar.
Repeat review of references on 22 Aug 2009

Dr Link's search strategy
Two different search strategies have been pursued, both targeting the same population: cardiac arrest, heart arrest, cardiopulmonary, resuscitation, post-cardiac arrest, and postresuscitation (textword and MeSH headings when applicable).
As for the intervention, search strategy #1 focused on the keywords arrhythmia, anti-arrhythmic, and unstable (MeSH headings when applicable), while search strategy #2 looked at prophylactic use of single antiarrhythmic agents.
Database searched: PubMed, Cochrane Library (including Cochrane database for systematic reviews and Cochrane Central Register of Controlled Trials), Embase, and AHA EndNote Master Library.
Moreover, cross-references from articles and reviews, and forward search using SCOPUS and Google scholar are ongoing.
Details of search are reported below.
PubMed
Search strategy #1: (("Heart Arrest"[Mesh]) OR (cardiac arrest) OR (cardiopulmonary resuscitation) OR ("Resuscitation"[Mesh])) AND ((Arrhythmia) OR (Anti-Arrhythmic) OR (Unstable)) AND ((Post-Cardiac Arrest) OR (postresuscitation))
Search strategy #2: ((("Amiodarone"[Mesh]) OR ("Lidocaine"[Mesh]) OR ("Procainamide"[Mesh]) OR ("Magnesium Sulfate"[Mesh]) OR ("Diltiazem"[Mesh]) OR ("Verapamil"[Mesh]) OR ("Digoxin"[Mesh]) OR ("Flecainide"[Mesh]) OR ("Propafenone"[Mesh]) OR ("Sotalol"[Mesh]) OR ("esmolol"[Substance Name]) OR

("Atenolol"[Mesh]) OR ("Metoprolol"[Mesh]))) AND (((prophylactic) OR (Post-Cardiac Arrest) OR (postresuscitation))) AND ((("Resuscitation"[Mesh]) OR ("Cardiopulmonary Resuscitation"[Mesh]) OR (cardiopulmonary resuscitation) OR ("Heart Arrest"[Mesh]) OR (cardiac arrest)))
Cochrane
Search strategy #1: ((prophylac*):ti,ab,kw) AND ((Arrhythmia):ti,ab,kw) OR ("Anti-Arrhythmia Agents"[Mesh])) AND ("Heart Arrest"[Mesh]) OR ("Cardiopulmonary Resuscitation"[Mesh])
Search strategy #2: single antiarrhythmic agents[Mesh] AND prophylac* AND ("Heart Arrest"[Mesh]) OR ("Cardiopulmonary Resuscitation"[Mesh])
Embase
Search strategy #1: (("Heart Arrest"[Mesh]) OR ("Resuscitation"[Mesh])) AND ((Arrhythmia[Mesh]) OR (Anti-Arrhythmic[Mesh]) OR (Unstable[Mesh])) AND ((Post-Cardiac Arrest) OR (postresuscitation))
Search strategy #2: (single antiarrhythmic agents [Mesh]) AND (((prophylactic) OR "Prophylaxis"[Mesh]) OR (Post-Cardiac Arrest) OR (postresuscitation))) AND ("Heart Arrest"[Mesh]) NOT (resuscitation)
EndNote
Search strategy #1: (Cardiac Arrest OR Resuscitation) AND (Arrhythmia OR Anti-Arrhythmic OR Unstable) AND (Post-Cardiac Arrest OR postresuscitation)
Search strategy #2: (single antiarrhythmic agents) AND (prophylactic OR Prophylaxis OR Post-Cardiac Arrest OR postresuscitation) AND (Cardiac Arrest OR Resuscitation)
And find articles which cite: "Dorian P, et al. Amiodarone as compared with lidocaine for shock resistant ventricular fibrillation. NEJM 2002; 346: 884-90 or Kudenchuk P, et al. Amiodarone for resuscitation after out of hospital cardiac arrest due to ventricular fibrillation. NEJM. 1999; 342: 871-878.

Task force comments included. Combined submission with Dr Mark Link

- **State inclusion and exclusion criteria**

Inclusion criteria included: human studies of adult cardiac arrest and anti-arrhythmic agents, peer-review
Exclusion criteria included: review articles and case reports, case series, not pertinent studies.

- **Number of articles/sources meeting criteria for further review:**

PubMed "heart arrest" or "cardiopulmonary resuscitation" " or "cardiac arrest" as MESH (headings) AND "Anti-Arrhythmia Agents" or "Lidocaine" or "Lignocaine" or "procainamide" or "amiodarone" or "bretylium" or "magnesium" as textword in abstract 185 articles

On further evaluation of relevant articles:

25 studies met inclusion criteria for further review. Of these 9 were LOE 1, 2 LOE 2, 2 LOE 3, 5 LOE 4, 7 LOE 5.

# Summary of evidence

## Evidence Supporting Clinical Question

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|---|---|---|---|---|---|
| **Good** | **{Dorian, 2002, 884} B (amiodarone vs lidocaine) {Kudenchuk, 1999, 871} B (amio vs lido)** | | | | |
| **Fair** | **{Nowak, 1981, 404} B (bretylium vs placebo)** | **Herlitz, 2003, 25 (lido vs no lido) {Herlitz, 1997, 199} A (lidocaine vs no lidocaine)** | | | **{Gorgels, 1996, 43} E (procainamide vs lido {Somberg, 2002, 853} B (amio vs lido)** |
| **Poor** | | **{Ohshige, 2005, 53} C (lidocaine vs no lidocaine)** | | | |
| | **1** | **2** | **3** | **4** | **5** |
| **Level of evidence** | | | | | |

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
*Italics = Animal studies*

## Evidence Neutral to Clinical question

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|---|---|---|---|---|---|
| **Good** | **{Allegra, 2001, 245} A (Mg vs placebo) {Hassan, 2002, 57} A (Mg vs placebo) {Olson, 1984, 807} B (Bretylium vs Lido) {Haynes, 1981, 353} C (bretylium vs lido)** | | | | |
| **Fair** | **{Kovoor, 2005, 518} C (sotalol vs lignocaine) {Thel, 1997, 1272} A (Mg vs placebo)** | **{Pollak, 2006, 199} C (amio vs lido) {Rea, 2006, 1617} E (amio vs lido) {Stiell, 1995, 264} B** | **{Tahara, 2006, 442} B (nifekalant vs lido)** | **{Skrifvars M 2004, 582} E (amio)** | **{Kowey, 1995, 3255} E (amio vs lido) {Levine JH 1996, 67} E (amio)** |

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|---|---|---|---|---|---|
| | **{Fatovich, 1997, 237} A (Mg vs placebo) {Weaver, 1990, 2027} B (lido vs epi)** | **(bretylium, lido, procainamide )** | | | |
| **Poor** | | | | | |
| | **1** | **2** | **3** | **4** | **5** |
| **Level of evidence** | | | | | |

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
*Italics = Animal studies*

# Evidence Opposing Clinical Question

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|---|---|---|---|---|---|
| **Good** | | | | | |
| **Fair** | | **{van Walraven, 1998, 544} B (lido vs no lido)** | **{Weaver, 1990, 2027} B (lido vs no lido)** | **{Hallstrom, 1991, 1025} C (quinidine, proc vs no antiarrhythmic)** | **{Nademanee, 2000, 742} C (amio, proc, bretylium vs no antiarrhythmic {Tomlinson D 2008, 15} E (amio)** |
| **Poor** | | | | | |
| | **1** | **2** | **3** | **4** | **5** |
| **Level of evidence** | | | | | |

A = Return of spontaneous circulation
B = Survival of event
C = Survival to hospital discharge
D = Intact neurological survival
E = Other endpoint
*Italics = Animal studies*

**REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:**

"In adult cardiac arrest (asystole, pulseless electrical activity, pulseless VT and VF) (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of antiarrhythmic drugs (lidocaine, procainamide, amiodarone, bretylium, magnesium) or combination with other drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. ROSC, survival) (O)."?

This is a revision of worksheet 21 from ILCOR 2005.
We have divided the three time frames of resuscitation and treatment into:
1) During resuscitation
2) After admission to the hospital/ED (implying ROSC has returned)
3) Prior to hospital discharge and continuing long-term (implying patient recovery)
Our question and the focus of this worksheet, ALS-D-025, addresses the first time frame. Another worksheet questions addresses time frame 2. There is no specific worksheet question which address time frame

There are actually several parts to this question, and we have divided the evidence according to the type of antiarrhythmic drugs being studied in various publications. However we should note that nearly all of the studies report interventions for Ventricular Fibrillation (VF) and pulseless Ventricular Tachycardia (VT) rather than for asystole or PEA. Only one study (Nowak, 1981) included patients in asystole or PEA. Evidence from Randomised Controlled Trials (RCT) is scant, and most of the studies use another antiarrhythmic drug as a control, rather than a placebo or no treatment. Thus, conclusions are limited to the relative effectiveness of antiarrhythmic drugs.

Studies looking at the use of Lidocaine in adult cardiac arrest:
{Herlitz, 1997, 199} LOE2, Fair Quality, Supporting – OHCA retrospective review, looking at the use of Lidocaine for VF. Reported increased ROSC with lidocaine
{Ohshige, 2005, 53} LOE2, Poor Quality, Supporting – OHCA controlled trial, looking at the use of Lidocaine for VF. Found increased survival in the group treated with lidocaine
{Kovoor, 2005, 518} LOE1, Fair Quality, Neutral - OHCA RCT looking at the use of Lidocaine vs Sotalol for VF. Reported no difference in ROSC.
{Weaver, 1990, 2027} LOE 1, Fair Quality, Neutral (lidocaine vs epinephrine) and LOE 3, Fair Quality, Opposing - OHCA, looking at the use of lidocaine vs bicarbonate for VF. Reported decreased survival to admission with lidocaine.
{Tahara, 2006, 442} LOE3, Fair Quality, Neutral - OHCA historical controls, looking at the use of nifekalant and lidocaine for VF. Reported decreased survival to admission for lidocaine
{van Walraven, 1998, 544} LOE2, Fair Quality, Opposing – In-hospital, retrospective review, looking at the use of Lidocaine for VF. Reported decreased survival to 1h associated with lidocaine

Studies looking at the use of Amiodarone in adult cardiac arrest:
{Kudenchuk, 1999, 871} LOE1, Good Quality, Supporting – OHCA RCT looking at the use of Amiodarone vs placebo (although 92% of placebo group received antiarrhythmic drugs, predominantly lidocaine, before randomization and 82% received antiarrhythmic drugs after randomization) for VF. Reported improved survival to admission for Amiodarone.
{Levine JH 1996, 67} LOE5, Fair Quality, Neutral - Trial in which in-patients with recurrent sustained hypotensive VT or VF who had failed treatment with procainamide, lidocaine and bretylium were given one of three doses of IV amiodarone. Of 273 patients 40% survived 24 hours without another arrhythmic episode. There was no clear difference between the three different doses of amiodarone.
{Skrifvars M 2004, 582} LOE 4, Fair Quality, neutral- Retrospective case series of IV amiodarone use in Helsinki which shows that undiluted amiodarone can be used safely.

{Tomlinson D 2008, 15} LOE 4, Fair Quality, Opposing- Small retrospective case series of patients with hemodynamically tolerated VT in which IV amiodarone terminated VT in 6/41 patients within 20 minutes, and 12/41 within 1 hour.
Studies looking at the use of Magnesium in adult cardiac arrest:
{Allegra, 2001, 245} LOE1, Good Quality, Neutral , {Hassan, 2002, 57} LOE1, Good Quality, Neutral – Prehospital RCT looking at the use of Mg vs placebo for VF Reported no difference in ROSC
{Thel, 1997, 1272} LOE1, Fair Quality, Neutral - ICU, RCT, looking at the use of Mg vs placebo for VF. Reported no difference in ROSC
{Fatovich, 1997, 237} LOE1, Fair Quality, Neutral - ED RCT looking at the use of Mg vs placebo for VF. Reported no difference in ROSC

Studies looking at the use of Bretylium in adult cardiac arrest:
{Nowak, 1981, 404} LOE1, Fair Quality, Supporting – ED RCT, looking at the use of Bretylium vs placebo for all cardiac arrest rhythms. Found improved survival to admission for bretylium

Studies looking at the use of Procainamide & Lidocaine in adult cardiac arrest:
{Gorgels, 1996, 43} LOE5, Fair Quality, Supporting - Inhospital, randomized prospective, looking at the use of Procainamide vs Lidocaine for sustained VT. Reported improved termination of VT with Procainamide. Not all patients were in cardiac arrest.

Studies looking at the use of Procainamide & quinidine in adult cardiac arrest:
{Hallstrom, 1991, 1025} LOE4, Fair Quality, Opposing - OHCA , retrospective review, looking at the use of antiarrhythmics for VF. Reported that use of procainamide & quinidine was associated with decreased survival

Studies looking at the use of Bretylium & Lidocaine in adult cardiac arrest:
{Haynes, 1981, 353} LOE1, Good Quality, Neutral, {Olson, 1984, 807} LOE2, Good Quality, Neutral – OHCA, randomised trials, looking at the use of Bretylium vs Lidocaine for VF. Reported no difference in survival

Studies looking at the use of Bretylium & Amiodarone in adult cardiac arrest:
{Kowey, 1995, 3255} LOE5, Fair Quality, Neutral – Inhospital, prospective trial, looking at the use of Bretylium & Amiodarone for unstable VT or VF. However not all patients were in cardiac arrest. Reported no difference in survival to 48h.

Studies looking at the use of Lidocaine & Amiodarone in adult cardiac arrest:
{Dorian, 2002, 884} LOE1, Good Quality, Supporting – OHCA RCT looking at the use of Amiodarone vs Lidocaine for VF Reported improved survival to admission with Amiodarone.
{Rea, 2006, 1617} LOE2, Fair Quality, Neutral – Inhospital, retrospective review, looking at the use of Amiodarone vs Lidocaine for VF Reported no difference in survival to 24h
{Pollak, 2006, 199} LOE4, Fair Quality, Neutral – Inhospital, retrospective review, looking at the use of Amiodarone vs Lidocaine for VF. Reported no difference in survival.
{Somberg, 2002, 853} LOE 1, Fair Quality, Supporting – Inhospital RCT, looking at the use of Amiodarone vs Lidocaine for VT. Reported improved survival to 1h with Amiodarone

Studies looking at the use of Lidocaine-procainamide-bretylium in adult cardiac arrest:
{Stiell, 1995, 264} LOE2, Fair Quality, Neutral –Inhospital, retrospective review, looking at the use of antiarrhythmics for VF. Reported increased survival to 1h with procainamide, but no difference compared to patients who did not receive anti arrhythmic drugs with bretylium and lidocaine.

{Nademanee, 2000, 742} LOE 5, Fair Quality, Opposing – Inhospital, controlled trial, looking at the use of antiarrhythmics vs sympathetic blockade for prevention of VF. Reported decreased survival with antiarrhythmics compared to sympathetic blockade.

**Conclusion**

CONSENSUS ON SCIENCE:

Evidence from two randomized double-blind controlled studies {Kudenchuk, 1999, 871} LOE1, Good Quality and {Dorian, 2002, 884} LOE1, Good Quality, demonstrated improved survival to hospital admission with amiodarone (compared to lidocaine) for patients in refractory VT/VF in the out-of-hospital setting, but no improvement in overall survival.
An additional randomized double-blind controlled trial {Somberg, 2002, 853} LOE1, Fair Quality, demonstrated improved 1 hr survival with amiodarone (compared to lidocaine) for patients in VF and VT, in the in-hospital setting.
Other lower LOE data on amiodarone were generally neutral {Levine JH 1996, 67} LOE5, Fair Quality {Rea, 2006, 1617} LOE2, Fair Quality, {Pollak, 2006, 199} LOE2, Fair Quality.

These trials were performed before the benefits of hypothermia was known, thus they did not incorporate this now proven therapy which improves survival after ROSC. Whether survival to hospital discharge and neurologic survival could be improved with amiodarone and subsequent hypothermia is not known. If that is the case then a stronger argument for amiodarone could be made; if that is not the case then an argument could be made to not give an AAD at all.

With lidocaine, the evidence was mixed and most of the data were from trial with LOE 3 or lower. Evidence from a non-randomised prospective trial, {Ohshige, 2005, 53} LOE2, Poor Quality; showed improved survival to discharge, with lidocaine and epinephrine (compared to epinephrine alone) for patients in VF, in the out-of-hospital setting. A retrospective review, {Herlitz, 1997, 199} LOE2, Fair Quality; demonstrated improved survival to admission, with lidocaine (compared to standard treatment) for patients in VF, in the out-of-hospital setting.
However OHCA studies, {Weaver, 1990, 2027} LOE 3, Fair Quality and {Tahara, 2006, 442} LOE3, Fair Quality; and an inhospital retrospective review, {van Walraven, 1998, 544} LOE2, Fair Quality; suggested decreased survival to admission with lidocaine (compared with bicarbonate, nifekalant or standard treatment respectively) for patients in VF.
Lidocaine was also inferior to amiodarone in 2 studies, {Dorian, 2002, 884} LOE1, Good Quality, and {Somberg, 2002, 853} LOE1, Fair Quality, showing decreased survival to admission and 1h respectively, for patients in VF and VT respectively, in the in-hospital and out-of-hospital setting respectively.

Magnesium underwent 3 randomised placebo controlled trials, {Allegra, 2001, 245} LOE1, Good Quality, {Thel, 1997, 1272} LOE1, Fair Quality and {Fatovich, 1997, 237} LOE1, Fair Quality, and none demonstrated any increase in ROSC, for patients in VF, in the prehospital, Intensive Care Unit and Emergency Department setting respectively.

With Bretylium, evidence from 1 randomized double-blind controlled study {Nowak, 1981, 404} LOE1, Fair Quality, found improved survival to admission with bretylium (compared to placebo) for patients with VF or asystole in the ED setting. Another 2 randomised OOHA trials, {Haynes, 1981, 353} LOE1, Good Quality, Neutral and {Olson, 1984, 807} LOE1, Good Quality; were neutral.

Regarding procainamide, evidence was mixed. Evidence from a randomized prospective trial, {Gorgels, 1996, 43} LOE5, Fair Quality, found procainamide (compared to lidocaine) improved termination of spontaneously occurring monomorphic VT in the in-hospital setting.

Another retrospective review, {Stiell, 1995, 264} LOE2, Fair Quality, found procainamide was associated with increased survival to 1h in patients with VF in an in-hospital setting.
However another retrospective review, {Hallstrom, 1991, 1025} LOE4, Fair Quality, found procainamide and quinidine were associated with decreased survival in patients with VF in an out-of-hospital setting.
TREATMENT RECOMMENDATION:
Amiodarone may be considered for those who have refractory VT/VF, defined as VT/VF not terminated by defibrillation, or VT/VF recurrence in out of hospital cardiac arrest or inhospital cardiac arrest.
There is inadequate evidence to support or refute the use of lidocaine and other antiarrythmic agents in the same settings.

**Acknowledgements**:

Dr Peter Morley for his inputs

## *Citation List*

Allegra J, Lavery R, Cody R, Birnbaum G, Brennan J, Hartman A, et al. Magnesium sulfate in the treatment of refractory ventricular fibrillation in the prehospital setting. Resuscitation. 2001 Jun; 49 (3):245-9.
**Abstract:** OBJECTIVE: To determine if magnesium sulfate (MgSO(4)) improves outcome in cardiac arrest patients initially in ventricular fibrillation (VF). METHODS: Randomized, prospective, double blind, placebo-controlled, multicenter prehospital trial using 2 g of MgSO(4). Eligible patients were non-traumatic cardiac arrest patients (> or =18 years of age) presenting in VF. The protocol included those patients refractory to three electroshocks. Epinephrine and either 2 g of MgSO(4) or placebo (normal saline) were then administered. The primary outcome variable was return of spontaneous circulation (ROSC) in the field and a perfusing pulse on arrival at the ED. Secondary endpoints included admission to the hospital (ADMT) and hospital discharge (DISC). IRB approval was obtained at all participating centers. RESULTS: Total 116 patients (58 MgSO(4), 58 placebo) were enrolled during the period from 4/1992 to 10/96 with 109 available. There were no significant differences between the groups in baseline characteristics and times to cardio pulmonary resuscitation (CPR), advanced life support (ALS), and first defibrillation, except for time to study drug administration. There was no significant differences in ROSC (placebo, 18.5%, and MgSO(4), 25.5%, P=0.38), ADMT (placebo rate=16.7%, MgSO(4)=16.4%, P=1.0) or DISC (placebo rate=3.7%, MgSO(4)=3.6%, P=1.0). CONCLUSIONS: We failed to demonstrate that the administration of 2 g of MgSO(4) to prehospital cardiac arrest patients presenting in VF improves short or long term survival.
Research Support, Non-U.S. Gov't

LOE1, Good Quality, Neutral , – Prehospital RCT looking at the use of Mg vs placebo for VF Reported no difference in ROSC

Dorian P, Cass D, Schwartz B, Cooper R, Gelaznikas R, Barr A. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. The New England journal of medicine. 2002 Mar 21; 346(12):884-90
**Abstract:** BACKGROUND: Lidocaine has been the initial antiarrhythmic drug treatment recommended for patients with ventricular fibrillation that is resistant to conversion by defibrillator shocks. We performed a randomized trial comparing intravenous lidocaine with intravenous amiodarone as an adjunct to defibrillation in victims of out-of-hospital cardiac arrest. METHODS: Patients were enrolled if they had out-of-hospital ventricular fibrillation resistant to three shocks, intravenous epinephrine, and a further shock; or if they had recurrent ventricular fibrillation after initially successful defibrillation. They were randomly assigned in a double-blind manner to receive intravenous amiodarone plus lidocaine placebo or intravenous lidocaine plus amiodarone placebo. The primary end point was the proportion of patients who survived to be admitted to the hospital. RESULTS: In total, 347 patients (mean [+/-SD] age, 67+/-14 years) were enrolled. The mean interval

between the time at which paramedics were dispatched to the scene of the cardiac arrest and the time of their arrival was 7+/-3 minutes, and the mean interval from dispatch to drug administration was 25+/-8 minutes. After treatment with amiodarone, 22.8 percent of 180 patients survived to hospital admission, as compared with 12.0 percent of 167 patients treated with lidocaine (P=0.009; odds ratio, 2.17; 95 percent confidence interval, 1.21 to 3.83). Among patients for whom the time from dispatch to the administration of the drug was equal to or less than the median time (24 minutes), 27.7 percent of those given amiodarone and 15.3 percent of those given lidocaine survived to hospital admission (P=0.05). CONCLUSIONS: As compared with lidocaine, amiodarone leads to substantially higher rates of survival to hospital admission in patients with shock-resistant out-of-hospital ventricular fibrillation.
Research Support, Non-U.S. Gov't, Sponsored by Wyeth-Ayerst Laboratories

*Randomized double-blind trial comparing amiodarone (n=180) with lidocaine (n=167) for refractory VF/VT demonstrating that amiodarone leads to substantially higher rates of survival to hospital admission. Refractory VF was defined as VF that did not terminate after a series of 3 shocks, epinephrine and fourth shock or VF that recurred after successful defibrillation or VF that occurred for the first time when their initial cardiac arrest rhythm was asystole or PEA. The mean time interval from arrest to drug administration was 25 minutes.The treatment groups had similar clinical profiles. Following administration of amiodarone 22.8% of patients were admitted alive, as compared to 12.0% in the lidocaine group (p=0.009; odds ratio, 2.17). However, there was no difference in survival to hospital discharge. Among the 41 patients who survived to hospital admission after receiving amiodarone, 9 (5 percent of the entire group) survived to hospital discharge, as compared with 5 of the 20 initial survivors in the lidocaine group (3 percent of the entire group, P= 0.34). In addition, there was no placebo group, thus whether amiodarone was beneficial or lidocaine harmful could not be ascertained.*

*LOE 1, good quality, neutral for question which includes all antiarrhythmic drugs, but does show superiority of amidarone over lidocaine, B*

Fatovich DM, Prentice DA, Dobb GJ. Magnesium in cardiac arrest (the magic trial). Resuscitation. 1997 Nov; 35(3):237-41.
**Abstract:** The prognosis of out of hospital cardiac arrest (OHCA) is dismal. Recent reports indicate that high dose magnesium may improve survival. A prospective randomized double blind placebo controlled trial was conducted at the emergency department (ED) of Royal Perth Hospital, a University teaching hospital. Patients with OHCA of cardiac origin received either 5 g MgSO4 or placebo as first line drug therapy. The remainder of their management was standard advanced cardiac life support (ACLS). Study endpoints were: (1) ECG rhythm 2 min after the trial drug; (2) return of spontaneous circulation; (3) survival to leave the ED; (4) survival to leave intensive care; and (5) survival to hospital discharge. Of 67 patients enrolled, 31 received magnesium and 36 placebo. There were no significant differences between groups for all criteria, except that there were significantly more arrests witnessed after arrival of EMS personnel in the magnesium group (11 or 35% vs 4 or 11%). Return of spontaneous circulation occurred in seven (23%) patients receiving magnesium and eight (22%) placebo. Four patients in each group survived to leave the ED and one from the magnesium group survived to hospital discharge. There were no survivors in the placebo group. In this study, the use of high dose magnesium as first line drug therapy for OHCA was not associated with a significantly improved survival. Early defibrillation remains the single most important treatment for ventricular fibrillation (VF). Further studies are required to evaluate the role of magnesium in cardiac and cerebral resuscitation.

LOE1, Fair Quality, Neutral - ED RCT looking at the use of Mg vs placebo for VF. Reported no difference in ROSC

Gorgels AP, van den Dool A, Hofs A, Mulleneers R, Smeets JL, Vos MA, et al. Comparison of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. Am J Cardiol. 1996 Jul 1;78(1):43-6.

**Abstract:** Efficacy of procainamide and lidocaine in terminating spontaneous monomorphic ventricular tachycardia (VT) was assessed in a randomized parallel study. Patients with acute myocardial infarction and those with poor hemodynamic tolerance of VT were excluded. Procainamide 10 mg/kg was given intravenously with an injection speed of 100 mg/min, and lidocaine was administered at an intravenous dose of 1.5 mg/kg in 2 minutes. Fourteen patients were randomized to lidocaine and 15 to procainamide. Termination occurred in 3 of 14 patients after lidocaine and in 12 of 15 patients after procainamide (p <0.01). Procainamide stopped 8 of 11 VTs not responding to lidocaine, and lidocaine stopped 1 of 1 not responding to procainamde. Of a total of 41 VT episodes, 4 of 15 responded to lidocaine and 20 of 26 to procainamide (p <0.01). Because of VT recurrences, 16 patients could be studied repeatedly with drugs given in the reversed order. This resulted in a total of 55 trials of 79 drug injections. Lidocaine terminated 6 of 31 VTs and procainamide 38 of 48 (p <0.001). The protocol was stopped in 4 cases because of adverse effects. A comparison of the QRS width and QT interval before and at the end of the injection revealed significant lengthening of these values after procainamide but no change after lidocaine. In conclusion, procainamide is superior to lidocaine in terminating spontaneously occurring monomorphic VT.

LOE 5, Fair Quality, Supporting - Inhospital, randomized prospective, looking at the use of Procainamide vs Lidocaine for sustained VT, not cardiac arrest. Reported improved termination of VT with Procainamide.

Hallstrom AP, Cobb LA, Yu BH, Weaver WD, Fahrenbruch CE. An antiarrhythmic drug experience in 941 patients resuscitated from an initial cardiac arrest between 1970 and 1985. Am J Cardiol. 1991 Oct 15;68(10):1025-31.

**Abstract:** Survival rates and antiarrhythmic drug use were determined in 941 consecutive patients resuscitated from prehospital cardiac arrest due to ventricular fibrillation between March 7, 1970, and March 6, 1985. Of these patients, 18.7% were treated for at least a portion of the period with quinidine, 17.5% with procainamide, and 39.4% received no antiarrhythmic agent. Beta blockers were prescribed for 28.3% of the patients. Unadjusted comparisons of survival estimates showed dramatically lower survival rates for patients who received antiarrhythmic drugs independent of beta-blocker therapy and significantly improved survival for patients receiving beta-blocker therapy independent of antiarrhythmic use. Patients for whom antiarrhythmic therapy was prescribed also had more adverse baseline risk factors, whereas patients taking beta blockers had fewer such risk factors. After adjustment for these baseline risk factors, the use of antiarrhythmics was weakly (p less than 0.09) associated with worsened survival; 2-year survival for procainamide-treated patients was 30% and quinidine-treated patients 55% (p = 0.003). Beta-blocker therapy was associated with improved (p less than 0.001) survival. Thus, although neither procainamide nor quinidine appear to have had a benefit on mortality, the effect of procainamide appears to be significantly worse than that of quinidine. The use of antiarrhythmic drug therapy in patients resuscitated from prehospital ventricular fibrillation should be regarded as not only unproved, but potentially hazardous, and should probably be restricted to testing in randomized clinical trials.

LOE4, Fair Quality, Opposing - OHCA , retrospective review, looking at the use of antiarrhythmics for VF. Reported that use of procainamide & quinidine was associated with decreased survival

Hassan TB, Jagger C, Barnett DB. A randomised trial to investigate the efficacy of magnesium sulphate for refractory ventricular fibrillation. Emerg Med J. 2002 Jan;19(1):57-62.

**Abstract:** BACKGROUND: Ventricular fibrillation (VF) remains the most salvageable rhythm in patients suffering a cardiopulmonary arrest (CA). However, outcome remains poor if there is no response to initial defibrillation. Some evidence suggests that intravenous magnesium may prove to be an effective antiarrhythmic agent in such circumstances. STUDY HYPOTHESIS: Intravenous magnesium sulphate given early in the resuscitation phase for patients in refractory VF (VF after 3 DC shocks) or recurring VF will significantly improve their outcome, defined as a return of spontaneous circulation (ROSC) and discharge from hospital alive. DESIGN: A randomised, double blind, placebo controlled trial. Pre-defined primary and

secondary endpoints were ROSC at the scene or in accident and emergency (A&E) and discharge from hospital alive respectively. SETTING, PARTICIPANTS, AND INTERVENTION: Patients in CA with refractory or recurrent VF treated in the prehospital phase by the county emergency medical services and/or in the A&E department. One hundred and five patients with refractory VF were recruited over a 15 month period and randomised to receive either 2-4 g of magnesium sulphate or placebo intravenously. RESULTS: Fifty two patients received magnesium treatment and 53 received placebo. The two groups were matched for most parameters including sex, response time for arrival at scene and airway interventions. There were no significant differences between magnesium and placebo for ROSC at the scene or A&E (17% v 13%). The 4% difference had 95% confidence intervals (CI) ranging from -10% to +18%. For patients being alive to discharge from hospital (4% v 2%) the difference was 2% (95% CI -7% to +11%). After adjustment for potential confounding variables (age, witnessed arrest, bystander cardiopulmonary resuscitation and system response time), the odds ratio (95% CI) for ROSC in patients treated with magnesium as compared with placebo was 1.69 (0.54 to 5.30). CONCLUSION: Intravenous magnesium given early in patients suffering CA with refractory or recurrent VF did not significantly improve the proportion with a ROSC or who were discharged from hospital alive.
Research Support, Non-U.S. Gov't

LOE1, Good Quality, Neutral – Prehospital RCT looking at the use of Mg vs placebo for VF Reported no difference in ROSC

Haynes RE, Chinn TL, Copass MK, Cobb LA. Comparison of bretylium tosylate and lidocaine in management of out of hospital ventricular fibrillation: a randomized clinical trial. Am J Cardiol. 1981 Aug;48(2):353-6.
**Abstract:** Bretylium tosylate was compared with lidocaine hydrochloride as initial drug therapy in 146 victims of out of hospital ventricular fibrillation in a randomized blinded trial. An organized rhythm was achieved in 89 and 93 percent and a stable perfusing rhythm in 58 and 60 percent of the patients who received bretylium and lidocaine, respectively. After initiation of advanced life support, an organized rhythm was first established after an average of 10.4 minutes and 10.6 minutes in the two respective groups, requiring an average of 2.8 defibrillatory shocks in those who received bretylium and 2.4 in the lidocaine-treated patients. Comparable numbers of patients were discharged from the hospital: 34 percent of those given bretylium and 26 percent of the patients whose initial therapy was lidocaine. No instance of chemical defibrillation was observed with either drug. In this study, bretylium afforded neither significant advantage nor disadvantage compared with lidocaine in the initial management of ventricular fibrillation.
Research Support, U.S. Gov't, P.H.S.

LOE1, Good Quality, Neutral, – OHCA, randomised trial, looking at the use of Bretylium vs Lidocaine for VF. Reported no difference in survival

Herlitz J, Ekstrom L, Wennerblom B, Axelsson A, Bang A, Lindkvist J, et al. Lidocaine in out-of-hospital ventricular fibrillation. Does it improve survival? Resuscitation. 1997 Jan;33(3):199-205.
**Abstract:** BACKGROUND: A large proportion of cardiac arrests outside hospital are caused by ventricular fibrillation. Although it is frequently used, the exact role for treatment with lidocaine in these patients remains to be determined. AIM: To describe the proportion of patients with witnessed out-of-hospital cardiac arrest found in ventricular fibrillation who survived and were discharged from hospital in relation to whether they were treated with lidocaine prior to hospital admission. Patients and treatment: All the patients with out-of-hospital cardiac arrest found in ventricular fibrillation in Goteborg between 1980 and 1992 in whom cardiopulmonary resuscitation (CPR) was initiated by our emergency medical service (EMS). During the observation period, some of the EMS staff were authorized to give medication and some were not. RESULTS: In all, 1,360 patients were found in ventricular fibrillation, with detailed information being available in 1,212

cases (89%). Lidocaine was given in 405 of these cases (33%). Among patients with sustained ventricular fibrillation, those who received lidocaine had a return of spontaneous circulation (ROSC) more frequently (P < 0.001) and were hospitalized alive more frequently (38% vs. 18%, P < 0.01). However, the rate of discharge from hospital did not significantly differ between the two groups. Among patients who were converted to a pulse-generating rhythm, those who received lidocaine on that indication were more frequently alive than those who did not receive such treatment (94% vs. 84%; P < 0.05). However, the rate of discharge did not significantly differ between the two groups. CONCLUSION: In a retrospective analysis comparing patients who received lidocaine with those who did not in sustained ventricular fibrillation and after conversion to a pulse-generating rhythm, such treatment was associated with a higher rate at ROSC and hospitalization but was not associated with an increased rate of discharge from hospital.
Research Support, Non-U.S. Gov't

LOE 2, Fair Quality, Supporting –*A retrospective study of the use of lidocaine in cardiac arrest. There was an inherent bias in who received lidocaine in this study because only ambulances with nurses on board could give lidocaine in the field. Yet the patients receiving lidocaine were more likely to survive to hospital admission, but not to hospital discharge.*

**Herlitz, J, Gunnarsson J, Engdahl J, et al Factors associated with survival to hospital discharge among patients hospitalized alive after out of hospital cardiac arrest: change in outcome over 20 years in the community of Goteborg, Sweden. Heart 2003. 89: 25-30.**

OBJECTIVE: To describe the change in survival and factors associated with survival during a 20 year period among patients suffering from out of hospital cardiac arrest and being hospitalised alive. PATIENTS: All patients hospitalised alive in the community of Goteborg after out of hospital cardiac arrest between 1 October 1980 and 1 October 2000 were included. METHODS: Patient data were prospectively computerised with regard to factors at resuscitation. Data on medical history and hospitalisation were retrospectively recorded. Patients were divided into two groups (the first and second 10 year periods). SETTING: Community of Goteborg, Sweden. RESULTS: 5505 patients suffered from cardiac arrest during the time of the survey. Among them 1310 patients (24%) were hospitalised alive. Survival (discharged alive) was 37.5% during the first part and 35.1% during the second part (NS). The following were independent predictors of an increased chance of survival: ventricular fibrillation/tachycardia as the first recorded rhythm (odds ratio (OR) 3.46, 95% confidence interval (CI) 2.36 to 5.07); witnessed arrest (OR 2.50, 95% CI 1.52 to 4.10); bystander initiated cardiopulmonary resuscitation (OR 2.00, 95% CI 1.42 to 2.80); the patient being conscious on admission to hospital (OR 6.43, 95% CI 3.61 to 11.45); sinus rhythm on admission to hospital (OR 1.53, 95% CI 1.12 to 2.10); and treatment with lidocaine in the emergency department (OR 1.64, 95% CI 1.16 to 2.31). The following were independent predictors of a low chance of survival: age > 70 years (median) (OR 0.65, 95% CI 0.47 to 0.88); atropine required in the emergency department (OR 0.35, 95% CI 0.16 to 0.75); and chronic treatment with diuretics before hospital admission (OR 0.59, 95% CI 0.43 to 0.81). CONCLUSION: There was no improvement in survival over time among initial survivors of out of hospital cardiac arrest during a 20 year period. Major indicators for an increased chance of survival were initial ventricular fibrillation/tachycardia, bystander cardiopulmonary resuscitation, arrest being witnessed, and the patient being conscious on admission. Major indicators for a lower chance were high age, requirement for atropine in the emergency department, and chronic treatment with diuretics before cardiac arrest.

*20 year retrospective review of survival in cardiac arrest. In multivariate analysis those give lidocaine in the ED had an improvement in survival (odds ratio of 1.64; 95% CI of 1.12 to 2.10).*

*LOE 2, ,retrospective, fair quality, supportive C*

Kovoor P, Love A, Hall J, Kruit R, Sadick N, Ho D, et al. Randomized double-blind trial of sotalol versus lignocaine in out-of-hospital refractory cardiac arrest due to ventricular tachyarrhythmia. Internal medicine journal. 2005 Sep;35(9):518-25.
**Abstract:** AIM: We aimed to compare the efficacy of sotalol versus lignocaine for the treatment of patients with out-of-hospital ventricular fibrillation refractory to > or = 4 defibrillatory shocks. BACKGROUND: The outcome of patients in ventricular fibrillation refractory to > or = 4 defibrillatory shocks is poor. In a previous randomized trial, sotalol was superior to lignocaine for acute termination of ventricular tachycardia not causing loss of consciousness. METHODS: Patients of the Ambulance Service of New South Wales treated by paramedics with continued ventricular fibrillation despite standard resuscitation and > or = 4 defibrillatory monophasic shocks were eligible. Drug doses were sotalol 100 mg or lignocaine 100 mg, given as i.v. boluses. A further 2 min of cardiopulmonary resuscitation was given and then defibrillation was repeated twice. If this failed, half the initial dose of the trial drug was repeated and a further > or = 2 shocks were given. RESULTS: Sixty patients were randomized to sotalol and 69 randomized to lignocaine. There was no significant difference between the two groups in the clinical characteristics of the patients or in the number of shocks received. Outcomes in the sotalol and lignocaine groups were survival to hospital admission in 7 (12%) and 16 (23%), respectively (P = 0.09), and survival to hospital discharge in 2 (3%) and 5 (7%), respectively (P = 0.33). CONCLUSIONS: Sotalol is not superior to lignocaine for treatment of ventricular fibrillation refractory to multiple shocks. The overall outcome of this group of patients is poor regardless of the pharmacological intervention (lignocaine or sotalol).
Research Support, Non-U.S. Gov't

LOE1, Fair Quality, Neutral – Small OHCA RCT looking at the use of Lidocaine vs Sotalol for VF. Reported no difference in ROSC.

Kowey PR, Levine JH, Herre JM, Pacifico A, Lindsay BD, Plumb VJ, et al. Randomized, double-blind comparison of intravenous amiodarone and bretylium in the treatment of patients with recurrent, hemodynamically destabilizing ventricular tachycardia or fibrillation. The Intravenous Amiodarone Multicenter Investigators Group. Circulation. 1995 Dec 1;92(11):3255-63.
**Abstract:** BACKGROUND: After several days of loading, oral amiodarone, a class III antiarrhythmic, is highly effective in controlling ventricular tachyarrhythmias; however, the delay in onset of activity is not acceptable in patients with immediately life-threatening arrhythmias. Therefore, an intravenous form of therapy is advantageous. This study was designed to compare the safety and efficacy of a high and a low dose of intravenous amiodarone with bretylium, the only approved class III antiarrhythmic agent. METHODS AND RESULTS: A total of 302 patients with refractory, hemodynamically destabilizing ventricular tachycardia or ventricular fibrillation were enrolled in this double-blind trial at 82 medical centers in the United States. They were randomly assigned to therapy with intravenous bretylium (4.7 g) or intravenous amiodarone administered in a high dose (1.8 g) or a low dose (0.2 g). The primary analysis, arrhythmia event rate during the first 48 hours of therapy, showed comparable efficacy between the bretylium group and the high- dose (1000 mg/24 h) amiodarone group that was greater than that of the low-dose (125 mg/24 h) amiodarone group. Similar results were obtained in the secondary analyses of time to first event and the proportion of patients requiring supplemental infusions. Overall mortality in the 48- hour double-blind period was 13.6% and was not significantly different among the three treatment groups. Significantly more patients treated with bretylium had hypotension compared with the two amiodarone groups. More patients remained on the 1000-mg amiodarone regimen than on the other regimens. CONCLUSIONS: Bretylium and amiodarone appear to have comparable efficacies for the treatment of highly malignant ventricular arrhythmias. Bretylium use, however, may be limited by a high incidence of hypotension.

LOE5, Fair Quality, Neutral – Inhospital, prospective trial, looking at the use of Bretylium & Amiodarone for unstable VT or VF. However not all patients were in cardiac arrest. Reported no difference in survival to 48h.

Kudenchuk PJ, Cobb LA, Copass MK, Cummins RO, Doherty AM, Fahrenbruch CE, et al. Amiodarone for resuscitation after out-of-hospital cardiac arrest due to ventricular fibrillation. The New England journal of medicine. 1999 Sep 16;341(12):871-8

**Abstract:** BACKGROUND: Whether antiarrhythmic drugs improve the rate of successful resuscitation after out-of-hospital cardiac arrest has not been determined in randomized clinical trials. METHODS: We conducted a randomized, double-blind, placebo-controlled study of intravenous amiodarone in patients with out-of-hospital cardiac arrest. Patients who had cardiac arrest with ventricular fibrillation (or pulseless ventricular tachycardia) and who had not been resuscitated after receiving three or more precordial shocks were randomly assigned to receive 300 mg of intravenous amiodarone (246 patients) or placebo (258 patients). RESULTS: The treatment groups had similar clinical profiles. There was no significant difference between the amiodarone and placebo groups in the duration of the resuscitation attempt (42+/-16.4 and 43+/-16.3 minutes, respectively), the number of shocks delivered (4+/-3 and 6+/-5), or the proportion of patients who required additional antiarrhythmic drugs after the administration of the study drug (66 percent and 73 percent). More patients in the amiodarone group than in the placebo group had hypotension (59 percent vs. 48 percent, P=0.04) or bradycardia (41 percent vs. 25 percent, P=0.004) after receiving the study drug. Recipients of amiodarone were more likely to survive to be admitted to the hospital (44 percent, vs. 34 percent of the placebo group; P=0.03). The benefit of amiodarone was consistent among all subgroups and at all times of drug administration. The adjusted odds ratio for survival to admission to the hospital in the amiodarone group as compared with the placebo group was 1.6 (95 percent confidence interval, 1.1 to 2.4; P=0.02). The trial did not have sufficient statistical power to detect differences in survival to hospital discharge, which differed only slightly between the two groups. CONCLUSIONS: In patients with out-of-hospital cardiac arrest due to refractory ventricular arrhythmias, treatment with amiodarone resulted in a higher rate of survival to hospital admission. Whether this benefit extends to survival to discharge from the hospital merits further investigation.
Research Support, Non-U.S. Gov't, Supported by the Medic One Foundation and by a grant from Wyeth–Ayerst Laboratories

LOE1, Good Quality, Supporting *Double-blind randomized controlled trial of amiodarone vs placebo in OOH VT or VF arrest resistant to 3 defibrillatory shocks. This study demonstrated an improved survival to hospital admission in patients administered amiodarone compared to placebo. Baseline characteristics of the 2 groups were similar (amiodarone n=246, placebo n=258).Elapsed time from arrest to amiodarone administration averaged 21.4 minutes. Post-ROSC hypotension or bradycardia were more frequent in the amiodarone group. Odds ratio favoring amiodarone for hospital admission was 1.6 (p=0.02). There was no difference in survival to hospital discharge (13.4 to 13.2%).*

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Levine JH,. Intravenous amiodarone for recurrent sustained hypotensive ventricular tachyarrhythmias. Intravenous Amiodarone Multicenter Trial Group. J. Am. Coll. Cardiol. 1996; 27: 67-75.

OBJECTIVES. We sought to determine the response rate and safety of intravenous amiodarone in patients with ventricular tachyarrhythmias refractory to standard therapies. BACKGROUND. Numerous small retrospective reports suggest a response of refractory ventricular tachyarrhythmias to intravenous amiodarone, yet no controlled prospective trials exist. METHODS. Two hundred seventy-three patients with recurrent hypotensive ventricular tachyarrhythmias refractory to lidocaine, procainamide and bretylium were randomized to receive one of three doses of intravenous amiodarone: 525, 1,050 or 2,100 mg/24 h (mean [+/- SE] dose 743.7 +/- 418.7, 1,175.2 +/- 483.7, 1,921.2 +/- 688.8 mg, respectively) by continuous infusion over 24 h. RESULTS. Of the 273 patients, 110 (40.3% response rate) survived 24 h without another hypotensive ventricular tachyarrhythmic event while being treated with intravenous amiodarone as a single agent (primary

end point). A significant difference in the time to first recurrence of ventricular tachyarrhythmia (post hoc analysis) over the first 12 h was observed when the combined 1,050- and 2,100-mg dose groups were compared with the 525-mg dose group (p = 0.046). The number of supplemental (150 mg) infusions of intravenous amiodarone (given for breakthrough destabilizing tachyarrhythmias) during hours 0 to 6 (prespecified secondary end point) was significantly greater in the 525-mg dose group than in the 2,100-mg dose group (1.09 +/- 1.57 vs. 0.51 +/- 0.97, p = 0.0043). However, there was no clear dose-response relation observed in this trial with respect to success rates (primary end point), time to first recurrence of tachyarrhythmia (post hoc analysis) or mortality (secondary end point) over 24 h. CONCLUSIONS. Intravenous amiodarone is a relatively safe therapy for ventricular tachyarrhythmias refractory to other medications.

LOE5, Fair Quality, Neutral - Trial in which in-patients with recurrent sustained hypotensive VT or VF who had failed treatment with procainamide, lidocaine and bretylium were given one of three doses of IV amiodarone. Of 273 patients 40% survived 24 hours without another arrhythmic episode. There was no clear difference between the three different doses of amiodarone.

Nademanee K, Taylor R, Bailey WE, Rieders DE, Kosar EM. Treating electrical storm : sympathetic blockade versus advanced cardiac life support-guided therapy. Circulation. 2000 Aug 15;102(7):742-7.

**Abstract:** BACKGROUND: Electrical storm (ES), defined as recurrent multiple ventricular fibrillation (VF) episodes, often occurs in patients with recent myocardial infarction. Because treating ES according to the Advanced Cardiac Life Support (ACLS) guidelines yields a poor outcome, we evaluated the efficacy of sympathetic blockade in treating ES patients and compared their outcome with that of patients treated according to the ACLS guidelines. METHODS AND RESULTS: Forty-nine patients (36 men, 13 women, mean age 57+/-10 years) who had ES associated with a recent myocardial infarction were separated into 2 groups. Patients in group 1 (n=27) received sympathetic blockade treatment: 6 left stellate ganglionic blockade, 7 esmolol, and 14 propranolol. Patients in group 2 (n=22) received antiarrhythmic medication as recommended by the ACLS guidelines. Patient characteristics were similar in the 2 groups. The 1-week mortality rate was higher in group 2: 18 (82%) of the 22 patients died, all of refractory VF; 6 (22%) of the 27 group 1 patients died, 3 of refractory VF (P<0.0001). Patients who survived the initial ES event did well over the 1-year follow-up period: Overall survival in group 1 was 67%, compared with 5% in group 2 (P<0.0001). CONCLUSIONS: Sympathetic blockade is superior to the antiarrhythmic therapy recommended by the ACLS guidelines in treating ES patients. Our study emphasizes the role of increased sympathetic activity in the genesis of ES. Sympathetic blockade-not class 1 antiarrhythmic drugs-should be the treatment of choice for ES.

LOE 5, Fair Quality, Opposing – Inhospital, controlled trial, looking at the use of antiarrhythmics vs sympathetic blockade for prevention of VF. Reported decreased survival with antiarrhythmics compared to sympathetic blockade.

Nowak RM, Bodnar TJ, Dronen S, Gentzkow G, Tomlanovich MC. Bretylium tosylate as initial treatment for cardiopulmonary arrest: randomized comparison with placebo. Annals of emergency medicine. 1981 Aug;10(8):404-7.

**Abstract:** To evaluate the therapeutic effectiveness of intravenous bretylium tosylate as a first-line drug for patients in cardiopulmonary arrest, a randomized, double-blind study was conducted, comparing bretylium with a normal saline placebo. Fifty-nine patients presenting to the emergency department with cardiopulmonary arrest due mainly to ventricular fibrillation or asystole initially received either bretylium (10 mg/kg) or placebo in a rapid intravenous bolus and were then otherwise treated according to standard American Heart Association guidelines. If ventricular fibrillation or asystole persisted, a second bolus of bretylium or normal saline was given after 20 minutes. Thirty-five percent of patients presenting with

ventricular fibrillation or asystole who received bretylium were successfully resuscitated, whereas 6% of patients who received placebo survived (P less than 0.05). These findings serve to suggest that the early use of bretylium tosylate in cardiopulmonary arrest improves survival.

LOE1, Fair Quality, Supporting – ED RCT, looking at the use of Bretylium vs placebo for all cardiac arrest rhythms. Found improved survival to admission for bretylium

Ohshige K, Shimazaki S, Hirasawa H, Nakamura M, Kin H, Fujii C, et al. Evaluation of out-of-hospital cardiopulmonary resuscitation with resuscitative drugs: a prospective comparative study in Japan. Resuscitation. 2005 Jul;66(1):53-61.
**Abstract:** OBJECTIVE: This study aimed at evaluating two emergency medical service systems, one in which emergency life-saving technicians (ELSTs) are allowed to administer epinephrine (adrenaline) to patients with out-of-hospital cardiac arrest and one in which ELSTs are allowed to administer epinephrine, lidocaine, and atropine. METHODS: A modified, prospective community health trial was conducted from April 1 to October 31, 2003. Areas served by physician-manned ambulances, where out-of-hospital cardiopulmonary resuscitation (CPR) was performed with resuscitative drugs (experimental areas), were compared to areas served by ELST-manned ambulances, where resuscitative drugs were not administered outside the hospital (reference areas). The sequence of emergency procedures performed in the experimental areas was divided into three phases. Phase I included administration of epinephrine, which simulated administration of epinephrine by ELSTs. Phase II started with the use of lidocaine or atropine. Phases I and II simulated administration of epinephrine, lidocaine, and atropine by ELSTs. Phase III began with administration of another drug. Outcomes, resuscitation rates and 1-month survival rates were determined, and differences between the two types of areas were analyzed. RESULTS: For non-traumatic cardiac arrest, outcomes through phase II in the experimental areas were significantly better than those in the reference areas. Phase I-only outcomes in the experimental areas were better, but not significantly better, than those in the reference areas. CONCLUSION: Use of resuscitative drugs for non-traumatic prehospital CPR appears to be effective in terms of resuscitation rates and 1-month survival rates.
Research Support, Non-U.S. Gov't

LOE2, Poor Quality, Supporting – OHCA controlled trial, looking at the use of Lidocaine for VF. *Ambulances manned with physicians who were allowed to use epinephrine, lidocaine and atropine were compared to ambulances manned without physicians. Survival was improved in those patients lucky enough to be cared for by a more advanced EMS system in which lidocaine was allowed. However, this study suffers from so many confounders that it offers little support for lidocaine*

Olson DW, Thompson BM, Darin JC, Milbrath MH. A randomized comparison study of bretylium tosylate and lidocaine in resuscitation of patients from out-of-hospital ventricular fibrillation in a paramedic system. Annals of emergency medicine. 1984 Sep;13(pt 2)(9):807-10.
**Abstract:** A prospective, randomized study using either bretylium tosylate (BT) or lidocaine (L) as the first-line antiarrhythmic for patients in refractory ventricular fibrillation was conducted using the Milwaukee County Paramedic System. If the patient did not respond to the initial American Heart Association protocol, BT (10 to 30 mg/kg total) or L (2 to 3 mg/kg total) was given randomly as the first antiarrhythmic. If the patient failed to convert, the alternate antiarrhythmic was given. In the L group, 81% (39/48) of the patients obtained an organized electrical rhythm and 56% (27/48) converted to a rhythm with a pulse. The resuscitation rate (admission to an emergency department with pulse) was 23% (11/48), and the save rate was 10.4% (5/48). In the BT group, 74% (32/43) obtained an organized electrical rhythm, 35% (15/43) were converted, 23% (10/43) were resuscitated, and 5% (2/43) were saved. The only significant difference in outcome was that L converted patients better than did BT (P less than .05). Of the 24 patients known to be on digitalis preparations

prior to arrest, 41% (5/12) in the L group were resuscitated and 16% (2/12) were resuscitated in the BT group. Data were analyzed for witnessed arrest outcome and for patients given multiple antiarrhythmics.

LOE1, Good Quality, Neutral – OHCA, randomised trials, looking at the use of Bretylium vs Lidocaine for VF. Reported no difference in survival

Pollak PT, Wee V, Al-Hazmi A, Martin J, Zarnke KB. The use of amiodarone for in-hospital cardiac arrest at two tertiary care centres. The Canadian journal of cardiology. 2006 Mar 1;22(3):199-202.
**Abstract:** BACKGROUND: Although amiodarone significantly increases survival to hospital admission when used in resuscitation of out-of-hospital pulseless ventricular tachycardia and fibrillation, there are limited data on its utility for in-hospital arrests. OBJECTIVES: To determine whether the use of amiodarone, as recommended by the year 2000 American Heart Association Advanced Cardiac Life Support guidelines, improved survival following its introduction to the resuscitation algorithm at two tertiary care institutions. METHODS: Charts of 374 cardiac resuscitations were retrospectively studied at the two institutions. Basic survival outcomes and demographic data were recorded for cardiac arrests with ventricular tachyarrhythmias qualifying for administration of antiarrhythmic agents. RESULTS: Qualifying rhythms were present in 95 patients. Clinical uptake of amiodarone was limited. In the 36 patients who received amiodarone, survival of resuscitation was 67% versus 83% (P=0.07) in the 59 patients receiving only other antiarrhythmic agents (chiefly lidocaine [94%]), while survival to discharge was 36.1% and 55.9% (P=0.06) in these two groups, respectively. CONCLUSIONS: Following two years' experience with the introduction of intravenous amiodarone for resuscitation in the institutions, use was less than 50% and no clinically observable survival benefit could be documented. Possible explanations for the difference between this experience and that found in out-of-hospital resuscitation trials include differing patient populations and operator bias during resuscitation. These results should provoke other institutions to question whether amiodarone has improved survival of cardiac arrest under the conditions prevailing in their hospitals. A patient registry or prospective, randomized trial will be required to assess what parameters affect the success of intravenous amiodarone for resuscitation in-hospital.
Research Support, Non-U.S. Gov't

LOE2, Fair Quality, Neutral *A retrospective study of in-hospital arrest. Inclusion criteria was VT or VF arrest. Of 95 patients, roughly a third received amiodarone and the remainder chiefly lidocaine. In this small study there was no difference in survival between the groups given amiodarone vs lidocaine*

Rea RS, Kane-Gill SL, Rudis MI, Seybert AL, Oyen LJ, Ou NN, et al. Comparing intravenous amiodarone or lidocaine, or both, outcomes for inpatients with pulseless ventricular arrhythmias. Critical care medicine. 2006 Jun;34(6):1617-23.
**Abstract:** OBJECTIVE: To compare survival rates of patients with in-hospital cardiac arrest due to pulseless ventricular tachycardia/ventricular fibrillation treated with lidocaine, amiodarone, or amiodarone plus lidocaine. DESIGN: Multicenter retrospective medical record review. SETTING: Three academic medical centers in the United States. PATIENTS: Hospitalized adult patients who received amiodarone, lidocaine, or a combination for pulseless ventricular tachycardia/ventricular fibrillation between August 1, 2000, and July 31, 2002. MEASUREMENTS AND MAIN RESULTS: Data were collected according to the Utstein style. In-hospital proportion of patients living at 24 hrs and discharge were analyzed using chi-square analysis. Of the 605 patient medical records reviewed, 194 met criteria for inclusion (n=79 for lidocaine, n=74 for amiodarone, n=41 for combination). Available data showed no difference in proportion of patients alive 24 hrs post-cardiac arrest (p=.39). Cox regression analysis indicated a decreased likelihood of survival in patients with pulseless ventricular tachycardia/ventricular fibrillation as an initial rhythm as compared with those who presented with

bradycardia followed by pulseless ventricular tachycardia/ventricular fibrillation and in those patients who received amiodarone as compared with lidocaine. However, only 14 patients (25%) in the amiodarone group received the recommended initial 300-mg intravenous bolus, and amiodarone was administered an average of 8 mins later in the code compared with lidocaine (p<.001). CONCLUSIONS: These results generate the hypothesis that inpatients with cardiac arrest may have different benefits from lidocaine and amiodarone than previously demonstrated. Inadequate dosing and later administration of amiodarone in the code were two confounding factors in this study. Prospective studies evaluating these agents are warranted.

LOE2, Fair Quality, Neutral – Inhospital, retrospective review, looking at the use of Amiodarone vs Lidocaine for VF Reported no difference in survival to 24h

Skrifvars M.B (2004) The use of undiluted amiodarone in the management of out-of-hospital cardiac arrest. Acta Anaesthesiol. Scand. 2004 48:5 (582 - 587)

Introduction: The Resuscitation 2000 Guidelines recommends amiodarone as the antiarrhythmic drug of choice in treatment of resistant ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT). Amiodarone has been associated with side-effects and difficulty of administration, due to recommended dilution, rendering it suboptimal for out-of-hospital cardiac arrest (CA) management. In the present study we report experiences and side-effects of the use of undiluted amiodarone in CA management in Helsinki Emergency Medical Service (EMS) during a 2-year period. Methods: On October 1, the Resuscitation 2000 Guidelines were put into practice in Helsinki EMS. Thus, in the cardiac arrest treatment protocol, after three ineffective shocks and 1 mg of adrenaline (epinephrine), a bolus of 300 mg of undiluted amiodarone (Cordarone®r 50 mg ml-1, Sanofi-Synthelabo, Helsinki, Finland) was administered into a vein located as centrally as possible. The Helsinki EMS performs systematic data collection according to the Utstein Guidelines. The blood pressure levels, heart rates and the need for vasopressors, of the patients with sustained return of spontaneous circulation (ROSC), were collected from the ambulance charts. Results: During October 1, 2000 and September 30, 2002, 712 patients were considered for resuscitation and 566 were resuscitated. The initial rhythms were as follows: 32% had VF/VT, 36% had asystole and 32% had pulseless electrical activity (PEA). Of the 180 patients with VF/VT, 75 (42%) received undiluted amiodarone in addition to other resuscitative measures. Of the patients with asystole or PEA, 12 (6%) and 18 (10%), respectively, received amiodarone. The blood pressure levels and the need vasopressors after ROSC and during transportation to the hospital were similar among the patients who received and those who did not receive amiodarone. Conclusions: The present study suggests that amiodarone can be administered undiluted without unmanageable haemodynamical side-effects in the treatment of out-of-hospital cardiac arrest. This is likely to save time and simplifies the treatment protocol in the prehospital setting.

LOE 4, Fair Quality, neutral, Retrospective case series of IV amiodarone use in Helsinki which shows that undiluted amiodarone can be used safely.

Somberg JC, Bailin SJ, Haffajee CI, Paladino WP, Kerin NZ, Bridges D, et al. Intravenous lidocaine versus intravenous amiodarone (in a new aqueous formulation) for incessant ventricular tachycardia. Am J Cardiol. 2002 Oct 15;90(8):853-9.

**Abstract:** The effectiveness of intravenous amiodarone for the treatment of incessant (shock resistant) ventricular tachycardia (VT) has not been established. This study evaluated the efficacy of a water-soluble amiodarone preparation or lidocaine for the treatment of shock-resistant VT. The trial was a double-blinded parallel design. Patients were randomized to receive up to 2 boluses of either 150 mg intravenous amiodarone or 2 boluses of 100 mg lidocaine followed by a 24-hour infusion. If the first assigned medication failed to terminate VT, the patient was crossed over to the alternative therapy. Twenty-nine patients were randomized to the study (18 received amiodarone and 11 received lidocaine). There were no significant differences between groups with regard to baseline characteristics. Immediate VT termination was achieved in 14 patients (78%)

with amiodarone versus 3 patients (27%) on lidocaine ($p < 0.05$). After 1 hour, 12 patients (67%) on amiodarone and 1 patient (9%) on lidocaine were alive and free of VT ($p < 0.01$). Amiodarone had a 33% drug failure rate, whereas there was a 91% drug failure rate for lidocaine. The 24-hour survival was 39% on amiodarone and 9% on lidocaine ($p < 0.01$). Drug-related hypotension with aqueous amiodarone was less frequent than with lidocaine. This study found that amiodarone is more effective than lidocaine in the treatment of shock-resistant VT.
Sponsored by Academic Pharmaceuticals, Lake Bluff, Illinois.

LOE 5, Fair Quality, *A very small multicenter double-blinded, parallel-designed, randomized trial evaluating the effectiveness of amiodarone (Amio-Aqueous) and lidocaine on shock resistant VT (lidocaine as control) Amiodarone was superior to lidocaine in: (1) termination of the VT, (2) survival at 1 hour, (3) survival at 24 hours (primary end point). However, there was no placebo group thus it is not clear whether amiodarone was beneficial or lidocaine harmful*

Stiell IG, Wells GA, Hebert PC, Laupacis A, Weitzman BN. Association of drug therapy with survival in cardiac arrest: limited role of advanced cardiac life support drugs. Acad Emerg Med. 1995 Apr;2(4):264-73.
**Abstract:** OBJECTIVE: To generate hypotheses regarding the association of standard Advanced Cardiac Life Support (ACLS) drugs with human cardiac arrest survival. METHODS: This observational cohort study was conducted over a two-year period in the wards, intensive care units, and EDs of two tertiary care hospitals. Included werc adult patients who suffered cardiac arrest either inside or outside the hospital and who required epinephrine according to standard ACLS guidelines. Six standard ACLS drugs (given while CPR was in progress) were assessed for association with survival from resuscitation to one hour and to hospital discharge by univariate and multivariate logistic regression analyses. RESULTS: In the 529 patients studied, initial cardiac rhythm had no impact on the association between drug administration and survival. The time of drug administration (quartile of ACLS period) was associated with resuscitation for atropine ($p < 0.05$) and lidocaine ($p < 0.01$). The odds ratios (95% CIs) for successful resuscitation, after multivariate adjustment for potential confounders, were: a respiratory initiating cause, 3.7 (2.1 -6.4); each 5-minute increase in CPR-ACLS interval, 0.5 (0.4-0.7); each 5-minute duration of ACLS. 0.9 (()1.8- 1.0; atropine, 1.2 (1.0-1.3); bretylium. (0.4 (0.1-1.1); calcium 0.8 (0.2-2.4); lidocaine, 0.9 (0.7-1.1); procainamide. 21.0 (5.2-84.0) d sodium bicarbonate 1.2 (1.0-1.6). All other potential confounding variables entered into the model were not significantly associated with resuscitation. CONCLUSION: Initiating cause of arrest, time to ACLS, and duration of ACLS were important correlates of survival. Other than procainaimide, standard ACLS drugs had relatively little association with survival, but timing of administration may be an important factor. Further research using definitive large randomized controlled trials is warranted to assess the role of drug therapy in improving cardiac arrest survival.
LOE 2, Fair Quality, Neutral –Inhospital, retrospective review, looking at the use of antiarrhythmics for VF. Reported increased survival to 1h with procainamide, but no difference compared to patients who did not receive anti arrhythmic drugs with bretylium and lidocaine.

Tahara Y, Kimura K, Kosuge M, Ebina T, Sumita S, Hibi K, et al. Comparison of nifekalant and lidocaine for the treatment of shock-refractory ventricular fibrillation. Circ J. 2006 Apr;70(4):442-6.
**Abstract:** BACKGROUND: Although nifekalant is a class III antiarrhythmic agent without negative inotropic activity, its effect in patients with shock-refractory ventricular fibrillation remains unclear. METHODS AND RESULTS: Patients who had an out-of-hospital cardiac arrest with ventricular fibrillation that persisted after 3 shocks from an external defibrillator, intravenous epinephrine, and another shock were retrospectively studied. The patients received lidocaine from January 1997 through June 2001 and nifekalant from July 2001 through December 2004. Short-term survival rates (survival to hospital admission and 24-h survival) were compared between the groups. The study group comprised 120 patients (mean age: 62+/-16 years): 55 received nifekalant

and 65 received lidocaine. Age, sex, history of ischemic heart disease, whether arrest was witnessed or not and time to arrival at the hospital did not differ significantly between the groups. As compared with lidocaine, nifekalant was associated with significantly higher rates of survival to hospital admission (67% vs 37%, p<0.001) and 24-h survival (53% vs 31%, p=0.01). Multivariate analysis showed that treatment with nifekalant and early initiation of cardiopulmonary resuscitation were independent predictors of 24-h survival. CONCLUSIONS: As compared with lidocaine, nifekalant may improve short-term survival in patients with out-of-hospital cardiac arrest due to shock-refractory ventricular fibrillation.

LOE3, Fair Quality, Neutral - *Retrospective study evaluating 120 OOH cardiac arrest patients refractory to 3 shocks from a defibrillator, epinephrine and a 4th shock who then received nifekalant (a class III AAD) or lidocaine. Nifekalant administration was associated with better ROSC and 24 hour survival. However there was no control group, thus whether nifekalant was beneficial or lidocaine detremental could not be ascertained.*

Thel MC, Armstrong AL, McNulty SE, Califf RM, O'Connor CM. Randomised trial of magnesium in in-hospital cardiac arrest. Duke Internal Medicine Housestaff. Lancet. 1997 Nov 1;350(9087):1272-6.
**Abstract:** BACKGROUND: The apparent benefit of magnesium in acute myocardial infarction, and the persistently poor outcome after cardiac arrest, have led to use of magnesium in cardiopulmonary resuscitation. Because few data on its use in cardiac arrest were available, we undertook a randomised placebo-controlled trial (MAGIC trial). METHODS: Patients treated for cardiac arrest by the Duke Hospital code team were randomly assigned intravenous magnesium (2 g [8 mmoles] bolus, followed by 8 g [32 mmoles] over 24 h; 76 patients) or placebo (80 patients). Only patients in intensive care or general wards were eligible; those whose cardiac arrest occurred in emergency, operating, or recovery rooms were excluded. The primary endpoint was return of spontaneous circulation, defined as attainment of any measurable blood pressure or palpable pulse for at least 1 h after cardiac arrest. The secondary endpoints were survival to 24 h, survival to hospital discharge, and neurological outcome. Analysis was by intention to treat. FINDINGS: There were no significant differences between the magnesium and placebo groups in the proportion with return of spontaneous circulation (41 [54%] vs 48 [60%], p = 0.44), survival to 24 h (33 [43%] vs 40 [50%], p = 0.41), survival to hospital discharge (16 [21%] vs 17 [21%], p = 0.98), or Glasgow coma score (median 15 in both). INTERPRETATION: Empirical magnesium supplementation did not improve the rate of successful resuscitation, survival to 24 h, or survival to hospital discharge overall or in any subpopulation of patients with in-hospital cardiac arrest.
Research Support, Non-U.S. Gov't

LOE1, Fair Quality, Neutral - ICU, RCT, looking at the use of Mg vs placebo for VF. Reported no difference in ROSC

Tomlinson, DR (2008) Intravenous amiodarone for the pharmacological termination of haemodynamically-tolerated sustained ventricular tachycardia: is bolus dose amiodarone an appropriate first-line treatment? Emergency Medicine Journal. 25(1):15-78
Objective: To examine the efficacy of bolus dose intravenous amiodarone for the pharmacological termination of haemodynamically-tolerated sustained monomorphic ventricular tachycardia (VT).
Design, setting and participants: Retrospective case series of consecutive emergency admissions with haemodynamically-tolerated sustained monomorphic VT administered bolus dose intravenous amiodarone 300 mg, according to current UK advanced life support practice guidelines.
Main outcome measures: Pharmacological termination rates within 20 min and 1 h and incidence of hypotension requiring emergency direct current cardioversion (DCCV) during this period.
Results: 41 patients (35 men) of mean (SD) age 68 (10) years, the majority (85%) with ischaemic heart disease and impaired left ventricular function (mean (SD) ejection fraction 0.31 (0.11)), were enrolled in the study.

The median VT duration was 70 min (range 15-6000), mean heart rate was 174 (34) bpm and systolic and diastolic blood pressures were 112 (22) and 73 (19) mm Hg, respectively. Pharmacological VT termination occurred within 20 min in 6/41 patients (15%; 95% CI 7% to 29%) and within 1 h in 12/41 patients (29%; 95% CI 18% to 45%). Haemodynamic deterioration requiring emergency DCCV occurred in 7/41 patients (17%; 95% CI 8% to 32%).
Conclusions: Although advocated by advanced life support guidelines, bolus dose intravenous amiodarone was relatively ineffective for acutely terminating haemodynamically-tolerated sustained monomorphic VT with a significant incidence of haemodynamic destabilisation requiring emergency DCCV. Previous studies in the identical clinical setting suggest that alternative antiarrhythmic agents, particularly intravenous procainamide and sotalol, may be superior. A prospective randomised trial is required to determine the optimal drug treatment for stable sustained monomorphic VT in the emergency setting.

LOE 4, Fair Quality, Opposing-Small retrospective case series of patients with hemodynamically tolerated VT in which IV amiodarone terminated VT in 6/41 patients within 20 minutes, and 12/41 within 1 hour

van Walraven C, Stiell IG, Wells GA, Hebert PC, Vandemheen K. Do advanced cardiac life support drugs increase resuscitation rates from in-hospital cardiac arrest? The OTAC Study Group. Annals of emergency medicine. 1998 Nov;32(5):544-53.
**Abstract:** STUDY OBJECTIVE: The benefit of Advanced Cardiac Life Support (ACLS) medications during cardiac resuscitation is uncertain. The objective of this study was to determine whether the use of these medications increased resuscitation from in-hospital cardiac arrest. METHODS: A prospective cohort of patients undergoing cardiac arrest in 1 of 5 academic hospitals was studied. Patient and arrest factors related to resuscitation outcome were recorded. We determined the association of the administration of ACLS drugs (epinephrine, atropine, bicarbonate, calcium, lidocaine, and bretylium) with survival at 1 hour after resuscitation. RESULTS: Seven hundred seventy-three patients underwent cardiac resuscitation, with 269 (34. 8%) surviving for 1 hour. Use of epinephrine, atropine, bicarbonate, calcium, and lidocaine was associated with a decreased chance of successful resuscitation (P <.001 for all except lidocaine, P <.01). While controlling for significant patient factors (age, gender, and previous cardiac or respiratory disease) and arrest factors (initial cardiac rhythm, and cause of arrest), multivariate logistic regression demonstrated a significant association between unsuccessful resuscitation and the use of epinephrine (odds ratio . 08 [95% confidence interval .04-.14]), atropine (.24 [.17-.35]), bicarbonate (.31 [.21-.44]), calcium (.32 [.18-.55]), and lidocaine (.48 [.33-.71]). Drug effects did not improve when patients were grouped by their initial cardiac rhythm. Cox proportional hazards models that controlled for significant confounders demonstrated that survivors were significantly less likely to receive epinephrine (P <. 001) or atropine (P <.001) throughout the arrest. CONCLUSION: We found no association between standard ACLS medications and improved resuscitation from in-hospital cardiac arrest. Randomized clinical trials are needed to determine whether other therapies can improve resuscitation from cardiac arrest when compared with the presently used ACLS drugs.

LOE2, Fair Quality, Opposing – Inhospital, retrospective review, looking at the use of Lidocaine for VF. Reported decreased survival to 1h associated with lidocaine

Weaver WD, Fahrenbruch CE, Johnson DD, Hallstrom AP, Cobb LA, Copass MK. Effect of epinephrine and lidocaine therapy on outcome after cardiac arrest due to ventricular fibrillation. Circulation. 1990 Dec;82(6):2027-34.
**Abstract:** One hundred ninety-nine patients with out-of-hospital cardiac arrest persisted in ventricular fibrillation after the first defibrillation attempt and were then randomly assigned to receive either epinephrine or lidocaine before the next two shocks. The resulting electrocardiographic rhythms and outcomes for each group of patients were compared for each group and also compared with results during the prior 2 years, a period when similar patients primarily received sodium bicarbonate as initial adjunctive therapy. Asystole occurred after defibrillation with threefold frequency after repeated injection of lidocaine (15 of 59, 25%)

compared with patients treated with epinephrine (four of 55, 7%) (p less than 0.02). There was no difference in the proportion of patients resuscitated after treatment with either lidocaine or epinephrine (51 of 106, 48% vs. 50 of 93, 54%) and in the proportion surviving (18, 19% vs. 21, 20%), respectively. Resuscitation (64% vs. 50%, p less than 0.005) but not survival rates (24% vs. 20%) were higher during the prior 2-year period in which initial adjunctive drug treatment for persistent ventricular fibrillation primarily consisted of a continuous infusion of sodium bicarbonate. The negative effect of lidocaine or epinephrine treatment was explained in part by their influence on delaying subsequent defibrillation attempts. Survival rates were highest (30%) in a subset of patients who received no drug therapy between shocks. We conclude that currently recommended doses of epinephrine and lidocaine are not useful for improving outcome in patients who persist in ventricular fibrillation.(ABSTRACT TRUNCATED AT 250 WORDS)
Research Support, Non-U.S. Gov't

LOE 1, Fair Quality, Neutral (lidocaine vs epinephrine); LOE 3, Fair, Opposing (Lidocaine versus bicarbonate infusion) - OHCA, looking at the use of lidocaine vs retrospective group using bicarbonate for VF. Reported decreased survival to admission with lidocaine.