

**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care****Worksheet author(s)**

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**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 "bretylum" 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 "bretylum" 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", "bretylum", "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 "bretylum" 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

Good	{Dorian, 2002, 884} B (amiodarone vs lidocaine) {Kudenchuk, 1999, 871} B (amio vs lido)				
Fair	{Nowak, 1981, 404} B (bretylium vs placebo)		{Herlitz, 1997, 199} A (lidocaine vs no lidocaine)	Herlitz, 2003, 25 (lido vs no lido)	{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

Good	{Allegra, 2001, 245} A (Mg vs placebo) {Hassan, 2002, 57} A (Mg vs placebo) {Haynes, 1981, 353} C (bretylium vs lido)	{Olson, 1984, 807} B (Bretylium vs Lido)			Haynes R 1981 C (bretylium vs lido)
Fair	{Kovoor, 2005, 518} C (sotalol vs lignocaine) {Thel, 1997, 1272} A (Mg vs placebo) {Fatovich, 1997, 237} A (Mg vs placebo)	{Tahara, 2006, 442} B (nifekalant vs lido)		{Rea, 2006, 1617} E (amio vs lido) {Pollak, 2006, 199} C (amio vs lido) {Stiell, 1995, 264} B (bretylium, lido, procainamide) {Skrifvars M 2004, 582} E (amio)	{Kowey, 1995, 3255} E (amio vs lido) {Levine JH 1996, 67} E (amio)
Poor					
	1	2	3	4	5
Level of evidence					

A = Return of spontaneous circulation

C = Survival to hospital discharge

E = Other endpoint

B = Survival of event

D = Intact neurological survival

*Italics = Animal studies*

### Evidence Opposing Clinical Question

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

A = Return of spontaneous circulation

C = Survival to hospital discharge

E = Other endpoint

B = Survival of event

D = Intact neurological survival

*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} LOE3, Fair Quality, Supporting – OHCA retrospective review, looking at the use of Lidocaine for VF. Reported increased ROSC with lidocaine
- {Ohshige, 2005, 53} LOE3, 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} LOE3, Fair Quality, Opposing - OHCA historical controls, looking at the use of lidocaine vs bicarbonate for VF. Reported decreased survival to admission with lidocaine
- {Tahara, 2006, 442} LOE2, 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} LOE4, 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  
 {The1, 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} LOE5, 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} LOE4, 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 5, 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} LOE4, 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.

**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.

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

*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 amiodarone over lidocaine, B*

Fatovich DM, Prentice DA, Dobb GJ. Magnesium in cardiac arrest (the magic trial). *Resuscitation*. 1997 Nov; 35(3):237-41.

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.

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.

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.

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.

LOE5, 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.

LOE4, 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.**

*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 4, ,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.

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.

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

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%).*

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

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.

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.

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.

LOE3, 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.

LOE2, 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.

LOE4, 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.

LOE4, 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)

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.

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.

LOE4, 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.

LOE2, Fair Quality, Neutral - *Retrospective study evaluating 120 OOH cardiac arrest patients refractory to 3 shocks from a defibrillator, epinephrine and a 4<sup>th</sup> 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 detrimental could not be ascertained.*

Theil 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.

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

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.

LOE4, 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.

LOE3, Fair Quality, Opposing - OHCA historical controls, looking at the use of lidocaine vs bicarbonate for VF. Reported decreased survival to admission with lidocaine