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

**Worksheet author(s)**

| Tommaso Pellis, MD | Date Submitted for review: January 13th 2010 |

**Clinical question.**

**ALS-D-019A** - In adult patients in monomorphic (wide complex) tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O)?

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** Intervention

**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).**

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 have been performed. Details of search are reported below.

**PubMed**

Search strategy #1: Tachycardia, Ventricular"[Mesh] AND "Treatment Outcome"[Mesh] AND (monomorphic OR wide complex)

Search strategy #2: Tachycardia, Ventricular/drug therapy"[Mesh] AND (monomorphic OR wide complex)

Result: 202 references

**Cochrane**

Search strategy #1: ((ventricular tachycardia):ti,ab,kw) AND (((monomorphic):ti,ab,kw) OR ((wide complex):ti,ab,kw)) AND ((therapy):ti,ab,kw)

Search strategy #2: (“Tachycardia, Ventricular”[MeSH]) AND (“Treatment Outcome”[MeSH]) AND ((monomorphic) OR (wide complex))

Result: 52 references

**Embase**

Search strategy: ((ventricular AND tachycardia) OR ('heart ventricle tachycardia'/exp) OR (ventricular AND 'tachycardia'/exp)) AND (('drug therapy'/exp) OR ('treatment outcome'/exp)) AND ((monomorphic OR (wide AND complex)) NOT (('cardioversion'/exp) OR (pacing))

Result: 202 references (151 non duplicates)

**EndNote**

Search strategy: (Ventricular AND Tachycardia) AND (monomorphic OR wide complex)

Result: 73 references (33 non duplicates)

**Others**

Cross-references from articles and reviews

Forward search using SCOPUS and Google scholar

The search strategy has been re-run on September 30th 2009.

**State inclusion and exclusion criteria**

Inclusion criteria: peer-review only, some reviews have been retained for bibliographic search.

Exclusion: pediatric and animal studies. Termination of arrhythmia by electrical (defibrillation, cardioversion, pacing, catheter ablation, etc) or mechanical means (precordial thump, fist pacing, cough, etc). Not pertinent studies (atrial fibrillation, cardiac resynchronization, polymorphic VT, programmed electrical stimulation induced VT). As well as induction and/or treatment of VT during an electrophysiological study (non-clinical VT).

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

37 studies met inclusion criteria for further review, of these 5 were classified as LOE 1, 2 as LOE 3, 23 of LOE 4, and 5 as LOE 5. Two are reviews.
# Summary of evidence

## Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Evidence</th>
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<th>Poor</th>
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<td><img src="E_lido" alt="Koster et al. 1985" /> ![Gorgels et al. 1996](E_proce vs lido) ![Ho et al. 1994](E_sot vs lido) ![Somberg et al. 2002](B_E_Amio vs lido)</td>
<td><img src="E_Amio" alt="Helmy et al. 1988" /></td>
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### Level of evidence

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

*Italicics = Animal studies*

In bold = references addressing onset of sustained stable mVT warranting prompt termination.

Not in bold = references relative to recurrent and refractory ventricular tachyarrhythmias

Lido = lidocaine  
Proc = procainamide  
Sot = sotalol  
Amio = amiodarone  
Ciben = cibenzalide  
Verap = verapamile  
β-block = β-blockers  
Bret = bretylium  
Nifek = nifekalant
### Evidence Neutral to Clinical question

<table>
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<td>[Berry et al. 1951] E^procain</td>
<td>[Brady et al. 1995]</td>
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**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

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<td>[Marill et al. 1997] E^Amio</td>
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<td>Poor</td>
<td>[Heng et al. 1975] E^verap</td>
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**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*
In adult patients in monomorphic (wide complex) tachycardia (prehospital and in-hospital) (P), does the use of any drug or combination of drugs (I) compared with not using drugs (or a standard drug regimen) (C), improve outcomes (eg. reversion rates) (O)?

Premises:
1) The present worksheet (WS) will focus exclusively on sustained wide complex tachycardia of ventricular origin.
2) Accurate differential diagnosis between supraventricular tachycardia and ventricular tachycardia (VT) is essential.
3) Correction of potentially causative or aggravating conditions such as hypokalemia and ischemia is an early priority.
4) DC shock is a reasonable alternative at any time, since timely termination is desirable even if monomorphic VT (mVT) is well tolerated. Although this should be regarded as a knowledge gap (i.e. there is no study investigating electrical vs. pharmacological strategy for sustained stable mVT) electrical cardioversion even at early stage or as “first line” is reasonable based on a prospective case series (LOE 4, fair quality)[van der Watt et al. 1995]. Indirect evidence is also provided by 3 LOE 4 studies of fair quality[Armengol et al. 1989, Desanctis 1965, Domanovits et al. 1999, 1997].

Antiarrhythmic drugs (AAD) are used to treat monomorphic sustained wide complex tachycardia in two very different settings/time frames which deserve separate analysis:
1) Acute onset of sustained stable mVT warranting prompt termination
2) Recurrent and refractory ventricular tachyarrhythmias: this is a long lasting condition (often days), including VT but comprising also polymorphic VT and ventricular fibrillation (VF), during which patients suffer from different degrees of hemodynamic compromise. Since the therapeutic approach varies, the two conditions will also be analyzed separately.

REVIEW
There are no placebo-controlled (LOE 1-3) studies specifically designed to address the effectiveness of antiarrhythmic drugs (AAD) in terminating monomorphic wide complex tachycardia. The 2005 guidelines suggested using amiodarone, procainamide or sotalol without recommending any medication over the other. Therefore it is not possible to define a standard drug regimen to be used as reference/control.

1) Acute termination

**Procainamide**
Procainamide has not been investigated in a placebo-controlled manner. Its utility for terminating VT has been suggested by a case series (LOE 4, poor quality) dating 1951[Berry et al. 1951]. Out of 11 patients with VT, 8 cardioverted to sinus rhythm during IV infusion of procainamide, suggesting a success rate of 73%. In further 6 cases of VT secondary to digitalis intoxication, procainamide terminated the arrhythmic event in 4. Hypotension was observed in all patients. In a randomized unblinded head-to-head trial (LOE 1, poor quality) between lidocaine and procainamide for termination of hemodynamically stable mVT, procainamide proved not only superior to lidocaine but exerted a very similar success rate to the above mentioned study[Gorgels et al. 1996]. Lidocaine 1.5 mg/kg in 2 min or procainamide 10 mg/kg at 100 mg/min were administered to 29 patients. If no response was observed after 15 min a cross over approach was performed and patients received the other drug. In case of VT recurrences the opposite order was used. Procainamide was more effective than lidocaine (12/15 vs 3/14, p < 0.01). When combining all VT occurrences, lidocaine was successful in 19% (6/31) and procainamide in 79% (38/48; p<0.001). The results are hampered by the lack of a true control group. Of notice patients with severe congestive heart failure or acute myocardial infarction (AMI) were excluded. At that dose and rate of infusion adverse effects were observed only in 2 patients receiving procainamide (hypotension and VT acceleration).

Hypotension following procainamide infusion is the main adverse effect. It is secondary to a direct negative inotropic effect, with changes in cardiac output, myocardial contractility and ultimately systemic blood pressure that are proportional to the dose as well as the rate of IV infusion[Jawad-Kanber et al. 1974].

**Lidocaine**
There is only one randomized-controlled trial (LOE 1, poor quality) in which subgroup analysis of patients developing VT after suspected AMI suggests that lidocaine is superior to placebo in terminating VT within 30 min[Koster et al. 1985]. The study was designed to demonstrate the efficacy of very early (pre-hospital) administration of intramuscular lidocaine in preventing primary VF in AMI patients. Hence, the results should be interpreted with caution and several limitations acknowledged: the study was not designed for subgroup analysis and to investigate the effect of lidocaine on VT which was not a preset endpoint. The results of subgroup analysis are further undermined by the small number of patients presenting VT (cardioversion occurred in 9/21 lidocaine-treated patients compared to 1/11 in the control group; p<0.05). The possible beneficial effect of lidocaine was confined to patients with confirmed AMI. Of note, while significantly reducing the number of VF episodes (2 vs. 12; primary endpoint), lidocaine did not impact on survival since advanced life support was promptly delivered, calling into question the prophylactic use of AADs per se. A patient self-injection prospective study with no controls (LOE 4, fair quality) reports a success rate of 36% following self intramuscular injection of 300 mg of lidocaine when telephone transmitted ECG was positive for mVT[Roth et al. 1997]. The lack of a control group does not allow to rule out spontaneous cardioversion and consequently the true effectiveness of lidocaine.

Disappointing results stem from two retrospective uncontrolled case series (LOE 4, fair quality)[Armengol et al. 1989, Marill et al. 1997]. Armengol et al.[Armengol et al. 1989] report a reversion rate of mVT of 19% (n=6/31). When lidocaine was not effective, alternative therapy was successful (electrical, 13 episodes; other AADs, 7) or VT spontaneously cardioverted few hours later (2 episodes). In the second study success rate of lidocaine was 17% (n=6/35), with history of prior MI being associated with failure to terminate VT (only 4.8% [1/21])[Marill et al. 1997]. Overall, cardioversion was successful in 16 of 18 attempts (89%). Consistently low rates of efficacy have been demonstrated by two head-to-head randomized trials, in which lidocaine was successful in 18% and 19% of cases[Gorgels et al. 1996, Ho et al. 1994].

Hypotension has been described following lidocaine administration.
Sotalol

Sotalol has not been investigated in a placebo-controlled manner. The efficacy of sotalol is supported by a double-blind randomized trial (LOE 1, poor quality)[Ho et al. 1994] comparing lidocaine to sotalol for termination of spontaneous-hemodynamically stable sustained mVT. Patients with AMI were included, approximately 50% of patients had LVEF <30%. Sotalol was more effective as first drug compared to lidocaine (69% vs 18%, which is 11/16 vs 3/17). Those with persistent VT 15 min after onset of administration of the first drug were crossed over to the other drug. VT was terminated in 7 of the 14 patients (50%) who crossed from lidocaine to sotalol and in 1 of 4 who crossed from sotalol to lidocaine (p=0.04). In none of the responders to sotalol (as first or second drug) did VT recur in the next 24 h. In 4 patients VT terminated spontaneously within 25 min after the overall 30 min study period. The second drug was sotalol in all these patients. The main limitation is dictated by the small numbers, however the study was prematurely terminated after interim analysis due to sotalol superiority. Nevertheless, the lack of a true control group hinders conclusions. Hypotension was observed in one patient per group, suggesting a similar safety profile even in patient with reduced cardiac function.

Amiodarone

Amiodarone has not been investigated in a controlled manner.

Three case series (LOE 4, fair quality) [Marill et al. 2006, Schutzenberger et al. 1989, Tomlinson et al. 2008] report on the use of amiodarone in altogether 93 cases of sustained hemodynamically stable mVT. Two studies examined reversion rates at 20 min from the start of IV infusion, success rate was 20% (15/74 patients)[Marill et al. 2006, Tomlinson et al. 2008]. Although the dose of amiodarone was double (300 mg) in the study by Tomlinson et al.[Tomlinson et al. 2008] the success rate reported was almost half (15%) of that reported by Marill and colleagues[Marill et al. 2006] (27%). According to two case series, using the same loading dose of 300 mg, the reversion rate at 60 min was 33% (20/60)[Schutzenberger et al. 1989, Tomlinson et al. 2008]. The overall reported success rate of amiodarone is 31% (29/93).

The population reported is mainly that of coronary artery disease patients (60% to 85%) with a mean LVEF ranging form 31 to 34%

Bearing in mind the limitations of retrospective case series with no controls or direct drug-to-drug comparison, altogether these three case series suggest that amiodarone might be less effective that procainamide or sotalol. Yet amiodarone seems to be the most studied drug for VT and probably the most widely used particularly because of the safety profile (i.e. less pro-arrhythmic effect than procainamide and impairment in ventricular function than sotalol) [Marill et al. 2006, Mooss et al. 1990, Schutzenberger et al. 1989, Tomlinson et al. 2008]

Bretylium

Bretylium has been omitted from the guidelines since the 2000 edition due to availability questions, its unfavorable side effect profile and the availability of safer agents that are at least as effective[Kowey et al. 1995]. Hence it shall not be considered here as well.

Verapamil

Based of 4 case series (LOE 4, fair quality) verapamil should not be administered to patients with mVT since it may promote hemodynamic deterioration and cardiac arrest[Buxton et al. 1987, Heng et al. 1975, Rankin et al. 1987, Stewart et al. 1986]. According to these studies in which VT was incorrectly diagnosed as supraventricular tachycardia and treated with IV verapamil, adverse effects ranged from 42% to 100%. Altogether over 81 cases reported, hypotension occurred in 63% (51/81), in 4 verapamil promoted VT acceleration, and other 4 patients experienced cardiac arrest (in 3 VT degenerated into VF, in 1 asystole).

Broad complex tachycardia associated with right bundle branch block, but without evidence of ischemic heart disease can be considered a specific clinical entity that comprises idiopathic left ventricular tachycardia. This peculiar and relatively rare condition (35 instances in 6 years at the Department of Emergency Medicine, Singapore General Hospital) responds well to verapamil according to a case series (LOE 4, fair quality), in which all but 1 patient (18/19, 95%) treated with verapamil (and/or diltiazem) were successfully cardioverted[Wang et al. 2002].

Cibenzoline

Cibenzoline has not been investigated in a controlled manner.

The only evidence available derives from a prospective double-site unblinded case series (LOE 4, fair quality) evaluating the safety and tolerability of IV cibenzoline for conversion of hemodynamically stable VT of recent onset[Chevalier et al. 1998]. Cibenzoline is an imidazoline derivative with potent antiarrhythmic properties and the electrophysiologic characteristics of type I, III and IV antiarrhythmic drugs. It has not been approved by the FDA, it is used only in some countries in Europe and Japan. When administered to 58 patients without AMI the reversion rate was 81% (47/58). Adverse effects observed were severe hypotension and proarrhythmia (one case each).

Electrical therapy was eventually required in 55% (8/33)[Marill et al. 2006] and 17% (7/41)[Tomlinson et al. 2008]. The three studies share the same main limitation, namely that an additive effect of prior administration of (multiple) AADs cannot be excluded since amiodarone was not used as first line drug. Only two case series report the rate of adverse effects. Hypotension occurred in 14% (10/74), requiring in all but one case electrical cardioversion due to hemodynamic deterioration[Marill et al. 2006, Tomlinson et al. 2008]. One case of asystole is also reported[Marill et al. 2006].

Cibenzoline is probably the most widely used particularly because of the safety profile (i.e. less pro-arrhythmic effect than procainamide and impairment in ventricular function than sotalol)

Recurrent and refractory ventricular tachyarrhythmias including mVT

Two randomized controlled trials (LOE 1, poor quality; but none placebo-controlled)[Kowey et al. 1995, Somberg et al. 2002] and seven LOE 4 studies (good to poor quality)[Helmy et al. 1988, Klein et al. 1988, Levine et al. 1996, Mooss et al. 1990, Morady et al. 1983, Ochi et al. 1989, Scheinman et al. 1995] have investigated the use of AADs in this clinical context. This condition comprises a heterogenous population of critically ill patients, not only in terms of ventricular arrhythmic events but also as far as hemodynamic status and number of AADs administered.
prior to or concomitantly to the study period. Severe underlying heart disease is frequently present. Although the definition of refractory recurrent ventricular arrhythmia varies from study to study, it can be summarized as follows:

- refractory to at least two AADs in the preceding 24-72 hrs
- at least 2 episodes of hemodynamically destabilizing VT or VF in the preceding 24 hours (on average much more frequent)
- need for multiple electrical cardioversion/defibrillation attempts

All but one study investigated the use of amiodarone, but none in a placebo-controlled randomized blinded fashion. The lack of a placebo-control group precludes the interpretation of true efficacy and quantification of the pharmacological success rate. With this limitation, taken together the case series (LOE 4, fair to poor quality)[Helmy et al. 1988, Klein et al. 1988, Mooss et al. 1990, Morady et al. 1983, Ochi et al. 1989] suggest that amiodarone is effective in reducing the number of life-threatening arrhythmia, shocks required and episodes of symptomatic sustained VT. The benefit can be quantified in a response rate (event free) at 24h of 58% (59/101)[Helmy et al. 1988, Klein et al. 1988, Mooss et al. 1990, Morady et al. 1983, Ochi et al. 1989] and at 48h of 76% (29/38) [Helmy et al. 1988, Ochi et al. 1989]. Data from methodologically more robust studies (double-blind randomized controlled trials [LOE 1, poor quality], or double-blind randomized dose-range studies [LOE 4, good quality]) indicate a lower efficacy of amiodarone, ranging from 26% to 40%[Levine et al. 1996, Scheinman et al. 1995, Somberg et al. 2002].

Besides one study (LOE 4, fair quality)[Ochi et al. 1989], the others report a significant incidence of adverse effects associated with amiodarone therapy, ranging from 13% to 42%[Helmy et al. 1988, Klein et al. 1988, Kowey et al. 1995, Levine et al. 1996, Mooss et al. 1990, Scheinman et al. 1995, Somberg et al. 2002]. Hypotension was the most frequent (7-26%), followed by symptomatic bradycardia, and a proarrhythmic effect secondary to QTc lengthening. Hypotension, associated with IV amiodarone, appears to be more dependent on the rate of drug administration than on the total amount of drug administered[Levine et al. 1996, Scheinman et al. 1995]. Pulmonary artery catheterization has been performed in 7 patients demonstrating a significant reduction in cardiac output in 6 during the initial bolus. The decline in cardiac output persisted at 60 min after the bolus and during the maintenance infusion. A tendency for a reduction in arterial pressure but that did not reach statistical significance was also reported[Klein et al. 1988].

There is only one study (LOE 4, fair quality)[Nademanee et al. 2000] that investigated the use of β-blocking agents in this context. Although flawed by several important limitations, this prospective study suggests that in patients with electrical storm, sympathetic blockade rapidly reduces life-threatening arrhythmias, improves short term survival and hospital discharge when compared to conventional ACLS-guided therapy[Nademanee et al. 2000]. The main criticisms to this study are: the absence of randomization (assignment to treatment protocol was based only on physician preference), ACLS-guided therapy relied on old antiarrhythmic knowledge according to the 1994 guidelines and, the sympathetic blockade group received when possible concomitant therapy with oral amiodarone.

Nifekalant

Nifekalant is a new class III AAD agent commercially available only in Japan. This drug has been initially studied as an alternative for lidocaine. Based on two LOE3 studies of good to fair quality [Ando et al. 2005, Yusu et al. 2009], one LOE4 [Kato et al. 2005] and one LOE5 study [Shiga et al. 2010] nifekalant appears promising in improving outcome in patients with shock refractory VF/VT although not as effective for immediate arrhythmia termination [Kato et al. 2005].

Acknowledgements:

Citation List


LOE 3, fair quality, supportive, E (Prolonged AAD treatment: nifekalant infusion)
This compared nifekalant to a historical control group in patients with ischemic heart disease and VF or VT. Most of the patients also received lidocaine. In the patients with VT immediate termination was achieved in just 1 out of 25 patients but nifekalant seemed efficient in preventing recurrence and seemed to be associated with increased survival.


LOE 4, fair quality, opposing, E (Acute termination).
A case series of 31 episodes of wide complex VT was obtained by retrospectively reviewing a computerized database of ECGs. Time period taken into consideration is not specified. Termination of tachycardia was considered to be temporally related to lidocaine when termination of arrhythmia occurred within 15 min from administration of one or more IV boluses. All but 3 pts had coronary artery disease. All but one case ware initially managed in the ED. Lidocaine boluses given ranged 75 to 400 mg. Termination of wide complex VT was temporally related to lidocaine administration in only 19% of cases (n=6/31). There was no difference in the dose of lidocaine administered between episodes that responded and those that did not. When not effective, alternative therapy was effective (cardioversion, 13; procainamide, 5; verapamil, 1; amiodarone, 1) or VT spontaneously cardioverted few hours later (2 episodes). When judged effective, response to lidocaine was not reproducible (n=2/5) or could be explained by concomitant therapy with other
drug (n=3/5). The authors conclude that lidocaine was usually ineffective for termination of sustained monomorphic VT. No reference to adverse effects of lidocaine administration is presented.

Arbitrarily considered opposing in light of the low success rate, but there is no evidence to support that lidocaine performs worst or better than placebo.

No comment about industry funding.


LOE 4, poor quality, supportive, E (Acute termination)
This is probably the first case series reporting the success of procainamide in terminating different arrhythmic events including VT. Out of 11 patients with VT, 8 cardioverted to SR during IV infusion of procainamide. In further 6 cases of VT secondary to digitalis intoxication, procainamide terminated the arrhythmic event in 4. Hypotension was observed in all patients.

No comment about industry funding.


LOE 5, poor quality, neutral, C
This is a retrospective prehospital chart review of adult patients who experienced out-of-hospital cardiopulmonary arrest with VT occurring at any time during resuscitation. The aim of the study was to determine the prevalence, response to therapy, and outcome of both monomorphic VT and polymorphic VT in the out-of-hospital cardiac arrest setting. Patients were treated according to 1987 American Heart Association ACLS Guidelines and antiarrhythmics administered with the intent of resuscitating a cardiac arrest victim. Hence the population is not the one of the worksheet question. The incidence of monomorphic VT as presenting rhythm was 8.7%.

No comment about industry funding.


LOE 4, fair quality, opposing, E (Acute termination)
A retrospective review of the records of patients referred to electrophysiology lab. 25 patients received IV verapamil (5 to 10 mg) in the ER as acute therapy for hemodynamically stable monomorphic VT. In each case VT was erroneously interpreted as supraventricular with aberrant conduction. VT was terminated by verapamil in 24% (6/25 patients). 44% of patients (11/25) experienced acute hemodynamic deterioration (VF developed in 3 pts). Seventeen of verapamil-treated patients had previous myocardial infarction. However, the 11 patients with verapamil-related adverse effects did not differ significantly from the 14 without them (including rate of underlying heart disease, VT morphology and ejection fraction). Review of 25 controls whose VT was treated with other antiarrhythmic agents revealed similar patient characteristics. Pharmacological cardioversion occurred in 52% (13/25), the remaining were successfully treated by electrically. Only 1 patient treated with bretylium experienced marked hypotension.

No comment on industry funding.


LOE 5, fair quality, neutral R (Prolonged AAD treatment: amiodarone infusion).
Review that elegantly summarizes the evidence supporting the use of amiodarone in the context of recurrent refractory ventricular tachyarrhythmia dominated by broad complex sustained VT.

No comment about industry funding.


LOE 4, fair quality, supportive, E (Acute termination).
Prospective double-site unblinded case series evaluating the safety and tolerability of IV cibenzoline for conversion of hemodynamically stable VT (SBP >90 mm Hg) of recent onset. Cibenzoline is an imidazoline derivative with potent antiarrhythmic properties and the electrophysiologic characteristics of type I, III and IV antiarrhythmic drugs. Yet it is used only in certain countries in Europe and in Japan, cibenzoline has not been FDA approved. In 6 years 58 patients met inclusion criteria, but none presented with acute myocardial ischemia. Out of 58 patients 47 (81%) were cardioverted by cibenzoline. There was no statistical difference between the responders and non-responders. Among the non responders (11), two (18%) developed cibenzoline-related side effects.
(hypotension, change in VT morphology). The authors conclude that this compound compared favorably with other intravenous antiarrhythmic drugs available but can not comment on the clinical application and the effect on VT during ongoing myocardial ischemia.

No comment about industry funding.


LOE 5, poor quality, neutral E (Acute termination).
A case series that first highlights the great effectiveness of DC-shocks when VT is not responding to antiarrhythmic agents. The novelty of the study lies in the use of electrical therapy even early, well before overt signs of hemodynamic decompensation. Only 8 of the 21 episodes were classified as hemodynamic unstable. Electrical therapy, although at that time its use was heterogeneous and ill defined (i.e. both AC and DC shocks at various energy range were used), was successful in 20/21 episodes of refractory VT.

No comment about industry funding.


LOE 4, quality, neutral, E (Acute termination).
A retrospective analysis of medical records of patients presenting at Vienna General Hospital ED with spontaneous sustained VT between December 1993 and August 1998. In 57 months, 75 patients presented with sustained VT: 58 hemodynamically stable, 17 unstable. Overall 77% of the patients were hemodynamically stable at presentation, underlining the fact that it is misleading to believe that VT always causes severe hemodynamic compromise. Out of the 58 stable 56 had monomorphic VT, while of the unstable 12 out of 17 had a monomorphic pattern. All unstable pts successfully responded to electrical therapy. Stable patients (including 2 polyVT) received a first line therapy with antiarrhythmic drugs (AAD): 3 (5%) cardioverted spontaneously before any therapy, 33 (57%) responded to drugs, 22 (38%) to second line electrical therapy. When administered, the success rate of AAD was 60%. Drug used were: lidocaine (28 pts, successful in 12), Ajmalin (8/15), Amiodarone (5/14), Sotalol (1/4), Propaphenone (0/1), Others (7/14). Again all patients treated with electrical therapy responded successfully (100%). The life threatening nature of VT is underlined by the fact that 7% of our patients died within 48 h and 17% still required intensive care after 48 h. Adverse drug effects are not reported. Follow up was max 48 h.

No comment about industry funding.


LOE 1, poor quality, supportive. E (Acute termination).
This is a randomized unblinded head-to-head trial between lidocaine and procainamide for termination of monomorphic hemodynamically stable VT. Patients with acute myocardial infarction, digitalis intoxication, severe liver or kidney disturbances, alcoholism or epilepsy were excluded.
Lidocaine 1.5 mg/kg in 2 min or procainamide 10 mg/kg at 100 mg/min were administered to 29 pts. If no response was observed after 15 min a cross over approach was used and pts received the other drug. In case of VT recurrences the opposite order was used. It is not specified over which time span the study was conducted. Results: procainamide was superior to lidocaine (12/15 vs 3/14, p < 0.01). When accounting also the second drug administration due to inefficacy of the first line agent, out of 41 VT episodes 4 of 15 responded to lidocaine and 20 of 26 to procainamide (p < 0.01). Overall, when considering also recurrent episodes, in 27 trials the first drug was lidocaine and in 28 procainamide. In 5 of the 27 patients VT responded to lidocaine in contrast to 22 of the 28 patients treated with procainamide (p < 0.001). Adverse effects were observed in 2 pts receiving lidocaine (hypotension) and 2 procainamide (hypotension & VT acceleration), all were classified as mild and quickly reversible. Limitations: patients with VT during acute ischemia or infarction were excluded, the study was unblinded, a carryover effect of one drug to the other cannot be excluded because only 15 minutes elapsed between subsequent drug injections. This study was arbitrarily considered supportive for procainamide, as lidocaine cant be considered a standard of therapy (not recommended as first line agent starting from 2000 Guidelines). The lack of a true control group hinders conclusions.
No comment about industry funding.


LOE 4, poor quality, supportive. E (Prolonged AAD treatment: amiodarone infusion)
Case series of patients with life-threatening recurrent sustained ventricular tachycardia (VT) or fibrillation (VF) that did not respond to at least two other antiarrhythmic drugs (AAD) and electrical therapy when appropriate. Previously administered medications are not specified. Amiodarone (5 mg/kg) was administered to 46 (consecutive?) patients over an unknown time period of
time as rescue pharmacological therapy. The exact type of ventricular arrhythmia is not reported. All is known is that 45 out of 46 patients required electrical cardioversion or defibrillation, on average 3 times in the 24 h before amiodarone administration. Following amiodarone administration 58.5% (27/46) were considered responders: 15 pts within 2 hours (33% of all pts), 26 pts within the first 72 h. In a subgroup with incessant VT during the 24 h before amiodarone administration the rate of success was similar: 9 pts (56%) responded to IV amiodarone, 5 (31%) within 2 h and 15 of 16 within the first 72 h. Side effects requiring treatment and/or discontinuation of AAD occurred in 6 pts (13%): hypotension being the most common (6), followed by sinus bradycardia requiring pacing (2) and QTc lengthening with development of polymorphic VT.

The study suffers from the following limitations, which by own admission of the authors, make it hard to distinguish between spontaneous resolution of arrhythmia and true therapeutic effect due to: a) absence of control group; b) long follow-up time and, c) unclear cause of arrhythmia. Finally of the 33 pts that responded (over 84 h follow-up) 15 received concomitant treatment with other AADs (not specified) adding further uncertainty in attributing the successful antiarrhythmic response to amiodarone.

No comment about industry funding.


LOE 4, poor quality, opposing, E (Acute termination).

In 5 patients with ventricular tachycardia (monomorphic?) verapamil was administered, in 4 as second or third line antiarrhythmic agent. Three patients were hemodynamically stable, 1 unstable, 1 arterial pressure not available (but HR 158). Sinus rhythm was restored in 1 patient. In 4 (including the only responder) hypotension followed drug administration. Of notice arterial pressure of the 5th patient was not provided. Information on patient selection criteria is unavailable.

No comment about industry funding.


LOE 1, poor quality, supportive, E (Acute termination).

This is a double-blind randomized trial comparing lidocaine to sotalol for termination of spontaneous sustained ventricular tachycardia (VT). Patients had to be conscious at the time of enrolment and were excluded if had a poor hemodynamic status which was judged to require DC shock. Drugs were administered over 5 min and considered effective if VT terminated within 15 min. Trial endpoints were termination of VT, hemodynamic collapse, persistence of VT even after administration of the second drug (cross-over design in case of failure of drug A). 17 patients were randomized to lidocaine and 16 to sotalol. The two groups had comparable baseline characteristics. Several patients had poor left ventricular function: 14 with LVEF < 30 of which 7 < 25%. Sotalol was more effective as the first drug (69% vs 18%, which is 11/16 vs 3/17). 1 patient in each group became hypotensive, lost consciousness and required electrical cardioversion. VT was terminated in 7 of the 14 patients (50%) who crossed from lidocaine to sotalol and in 1 of 4 who crossed from sotalol to lidocaine (p=0.04). In none of the responders to sotalol (as drug A or B) did VT recur in the next 24 h. 8 patients remained in VT and were cardioverted or managed with overdrive pacing. In 4 patients VT terminated spontaneously 1.5, 4, 15 and 25 min after the trial. Drug B was sotalol in these patients. Limits: patients randomized to lidocaine did not receive continuous infusion because the aim was acute cardioversion. The study was prematurely terminated at interim analysis due to sotalol superiority. Conclusion: sotalol was 3 to 4 times more effective than lidocaine and equally safe. This study was arbitrarily considered supportive for sotalol, as lidocaine cant be considered a standard of therapy (not recommended as first line agent starting from 2000 Guidelines). The lack of a true control group hinders conclusions. The study was independent of drug company funding. The same company markets both drugs in the state (Australia) were the study was conducted.


LOE 5, fair quality, neutral E (Dose safety study)

In this study evaluating cardiovascular effects of high doses of procainamide 14 patients were investigated: 7 has alcoholic cardiomyopathy, 4 mitral stenosis, 1 hypertensive heart, 1 mild aortic insufficiency, 1 traumatic myocardial contusion. infusion of 500 mg over 10 min led to blood levels 5 to 10 times therapeutic concentrations. This induced only a slight variation in heart rate, but a statistical reduction in cardiac index, LV stroke work, LV peak dp/dt. Although there was no significant reduction in systemic vascular resistance there was a reduction in mean aortic pressure. The study suggests that hypotension following procainamide infusion is secondary to a direct negative inotropic effect. Moreover, changes in cardiac output, myocardial contractility and systemic blood pressure were proportional to the dose as well as the speed of IV infusion.

No comment about industry funding.

LOE 4, good quality, supportive, E (Prolonged AAD treatment: nifekalant infusion).
In this study nifekalant does not seem to very effective in immediate conversion of a VT but seems to prevent re-occurrence.


LOE 4, fair quality, supportive E (Prolonged AAD treatment: amiodarone infusion).
Case series with no controls of 13 patients with recurrent VT that was refractory to at least 3 antiarrhythmic drugs (AAD) who were treated with IV amiodarone. Of the 13 patients 8 had required 5 to 16 electrical cardioversions for hemodynamically unstable VT or VF in the preceding 24 h. Amiodarone was administered as a bolus of 5 to 7.5 mg/kg over 15-20 min followed by an infusion of 10 mg/kg/24hrs for 24 to 72 hrs. In 7 of 13 patients (54%), all episodes of sustained VT or VF were suppressed. Pulmonary artery catheterization was performed in 7 patients demonstrating a significant reduction in cardiac output in 6 during the initial bolus. The decline in cardiac output persisted at 60 min after the bolus and during the maintenance infusion. There was a tendency for a reduction in arterial pressure but did not reach statistical significance. There were no significant changes in ECG parameters, although there was a tendency for prolonged QTc intervals. The initial bolus resulted in high amiodarone levels immediately after the bolus; these levels rapidly declined within 60 min. Maintenance infusion failed to sustain levels of 1 mg/ml or more in 4/9 patients at 60 min and in 5 at 120 min after initial bolus. Limitations: a) a possible synergistic or additive effect of concurrent use of other AAD can not be excluded, b) since there were no controls, termination of VT by spontaneous cardioversion can not be ruled out.
No comment about industry support.


LOE 1, poor quality, supportive, E (Acute termination).
In this prehospital double blind clinical trial, patients with suspected acute myocardial infarction (AMI) were randomly allocated to receive either intramuscular lidocaine (400 mg) or no injection at all (injection pen with no needle and drug). Treatment allocation was therefore immediately unblinded to health care providers and most likely to patients as well. The primary endpoint was prevention of ventricular fibrillation. In 33 months 6024 patients were randomized; acute AMI was diagnosed in 32% (n=1935), 34% of the lidocaine group and 31% of the control group (p<0.02). With this exceptions the two groups were comparable. After 15 min of injection - 10 min are necessary to obtain therapeutic plasma concentrations of lidocaine - the ventricular fibrillation was significantly reduced in the treatment group (2 vs. 12, p<0.01). However, there was no difference in survival due to prompt advanced life support in all but 1 VF episode. In a subgroup analysis of patients presenting with VT (n=32, AMI confirmed in 14, not specified whether mono or polymorphic) lidocaine was associated more frequently with VT termination within 30 min (n=9/21) than in the control group (1/11; p<0.05). Further sub-analysis suggests that lidocaine effect was confined to AMI patients (6/9 vs. 0/5, p=0.02). Of note the study was not designed for subgroup analysis and to investigate the effect of lidocaine on VT which was not a secondary endpoint. The results of subgroup analysis is further undermined by the small number of patients presenting with VT. No life threatening side effects were observed.
Supported by a grant (79-057) from The Netherlands Heart Foundation.


LOE 1, poor quality, neutral, B E, (Prolonged AAD treatment: amiodarone infusion).
A randomized, double-blind, parallel, positive-controlled, multicenter trial on patients with incessant (recurring immediately after termination) VT, VF, or at least 2 episodes of hemodynamically destabilizing VT or VF in the 24 hours before enrollment. All patients were refractory to or intolerant of lidocaine and propranolol in the 72 hours before enrollment. Patients were randomly assigned to 48 hours therapy with either IV bretylium (4.7 g) or IV high dose (1.8 g) or low dose (0.2 g) amiodarone. The primary endpoint was the event rate (events per unit time for the double-blind study period). Secondary analyses included time to first event, proportion of patients in each group free of arrhythmias at specified time points, and number of supplemental infusions administered during the double-blind period. Results: 302 patients were enrolled over a two year period (1990-1992). Baseline data from the three groups was comparable. There were no differences in the overall event rate among the treatment groups (P=.237). However, there were significant differences among the groups at the 6-hour time point (P=.049), and the differences approached significance at the 12-hour time point (P=.091). An analysis of event rates during the initial hours of drug administration indicated that >80% of all events occurred in the first 12 hours. There was a higher event rate for patients treated with the 125-mg/24-h dose of amiodarone. In
addition, >50% of the bretylum-treated patients discontinued blinded therapy before hour 16 and crossed over to open-label amiodarone. Although this study was not designed to determine the effects of these agents on the termination of arrhythmia, the incessant-VT population provided an opportunity to examine these effects. While not achieving statistical difference, the numerical differences among groups were seen in the median time from initiation of therapy to termination of incessant VT, as follows: bretylum, 6.98 hours (n=9); low-dose amiodarone, 4.58 hours (n=13); and high-dose amiodarone, 4.23 hours (n=12). Survival was comparable for all three treatment groups; 86% of the patients survived to 48 hours. During the 48-hour double-blind period, more patients (P=0.10) in the bretylum dose group (38%) had drug-related adverse effects compared with the 125-mg/24-h dose group (38%) or the 1000-mg/24-h dose group (42%). These included hypotension, congestive heart failure, and diarrhea; all were significantly more frequent in the bretylum-treated patients than in amiodarone-treated patients. During the first 6 and 12 hours, there were a significantly greater number of discontinuations from the bretylum dose group for both treatment failures and lack of efficacy than from the amiodarone dose groups (P=0.04 and P=0.36, respectively). By hour 15, more than 50% of the patients randomly assigned to bretylum had crossed over to open-label amiodarone. Limitations: there was no placebo arm limiting any definitive conclusion on hard end points such as 48-hour and 40-day mortality. The authors judged unethical to implement a placebo-controlled study in such a sick population. In conclusion, high dose amiodarone suppressed highly malignant ventricular arrhythmias in patients with severe underlying heart disease. This dose of amiodarone was at least as effective as bretylum, but better tolerated hemodynamically. Amiodarone appears to be more effective than bretylum during the first 12 hours of therapy. Supported by a grant from Wyeth-Ayerst Research.


LOE 4, good quality, neutral, B E (Prolonged AAD treatment: amiodarone infusion)
This is a multicenter randomized double-blind dose-range study to determine the response to IV amiodarone in patients with life-threatening hypotensive ventricular arrhythmias refractory to lidocaine, procaainamid, and bretylum in the prior 72 h. The time span of the study is not reported. Patients were randomized to 3 dose regimens over 24 h: 525 mg, 1050 mg, and 2100 mg. Placebo control group was deemed unethical by investigators. All pts had at least 2 episodes (mean 5.9) of hypotensive ventricular tachyarrhythmias in the 24 h before enrollment or were in incessant VT, despite attempts of cardioversion. Cardioversion was required in 80% of episodes, 15% required CPR, 51% resulted in loss of consciousness. The exact nature of arrhythmias is not further specified. Overall IV amiodarone was associated with apparent antiarrhythmic response in approx 40% of pts meeting study entry requirements (n=237). The study yet failed to demonstrate a dose-response to IV amiodarone in terms of proportion of pts who survived with a successful response (defined as no further episodes of VT/VF [primary endpoint] and no adverse drug effects during hours 6 to 24) or with respect to mortality. A significantly greater number of supplemental infusions of IV amiodarone (allowed by protocol at physician discretion; secondary endpoint) were administered, in the loading period of first 6 h, in the 500 mg group than in the 2000 mg group, suggesting a dose response relation. Amiodarone-related adverse effects occurred in 38% of patients (n=105). The frequency of adverse effects was similar among groups. Hypotension was the most common (15%, n=40), requiring vasopressor therapy in 14% (n=38) and leading to death in 2% (n=6). A proarhythmic effect was observed in 2% (n=6). Death rate did not differ significantly among groups. Limitations: by author admission the sample size was insufficient for the primary endpoint; lack of control group precludes the interpretation of true efficacy and quantification of success rate.
The study was supported by Wyeth-Ayerst Research, Radnor, Pennsylvania.


LOE 5, good quality, neutral, E.

A double blind randomized control trial on the efficacy of lidocaine in preventing primary ventricular fibrillation (VF) when administered early (within 6 h) to acute myocardial infarction patients. Although looking at a different setting and population (hence LOE 5) the study reports data on prevention of VT. 2 episodes in the treatment group (n=107) compared to 6 in the control group (n=105; p=ns). The primary endpoint of the study was prevention of VF which occurred only in the control group (0 vs. 9 episodes of VF; p<0.01), yet the overall mortality rate in both groups was comparable. Out of 9 patients that developed VF 8 were successfully defibrillated, the remaining patient was refractory to electrical and pharmacological therapy. The results of this study are therefore questionable, particularly in the current era of early b-blocker therapy that significantly improves mortality of AMI patients. Moreover, DWS5% was used as placebo making arguable this as a true control group since glycermic control has been shown to improve outcome in critical patients. Finally, at a dose of 100 mg bolus + 3 mg/min infusion for 48h the rate of lidocaine related adverse effects (drowsiness, dumbness of lips and tongue, speech disturbances, and dizziness) was as high as 15%, requiring a reduction in infusion rate in half. No comment on industry funding.

LOE 4, fair quality, neutral, E (Acute termination).
This is a retrospective case series of patients with sustained monomorphic ventricular tachycardia (VT) treated with IV amiodarone. Patients included presented with wide QRS complex tachycardia that was stable and sustained or recurrent, and received at least 150 mg amiodarone IV infusion during 15 minutes. Patients with polymorphic VT morphology were excluded from the study. The primary outcome was termination of VT within 20 minutes of onset of amiodarone infusion. Thirty-three patients who presented between 1996 and 2005 were enrolled. Ultimately, 9 patients experienced VT termination (27%) a median of 10 minutes (interquartile range 5.25 to 12.25) after initiation of amiodarone infusion. For the remaining 24 patients who received another treatment after amiodarone, the median time until the next treatment after initiation of amiodarone infusion was 25 minutes (interquartile range 20 to 42). Eighteen patients of 33 (55%), eventually required electrical therapy, including overdrive antitachycardia pacing, direct current cardioversion, or unsynchronized defibrillation for ventricular tachycardia termination. There were 4 patients with adverse effects that occurred after amiodarone infusion (3 hypotension, 1 asystole). Limitations: a) the risk of bias due to the retrospective nature of the study; b) therapeutic agents administered immediately before amiodarone may have also confounded the results.
The authors declare no conflict of interest and no external funding or support for this study.


LOE 4, fair quality, opposing, E (Acute termination).
A multicenter (5 institutions), retrospective analysis of the treatment of patients with spontaneous sustained stable VT between January 1990 and July 1996. Stable VT was defined as an uninterrupted rhythm for at least 5 minutes to ensure that spontaneous termination did not occur coincidentally with pharmacologic therapy. Drug efficacy was defined as conversion to a supraventricular rhythm within 15 minutes after the onset of lidocaine, procainamide, or bretylium therapy, or within 5 minutes of adenosine therapy. If VT recurred within 5 minutes after initial termination, then the treatment was considered unsuccessful. There were 40 cases of VT identified. The number of patients treated with drugs other than lidocaine was insufficient for meaningful analysis. The rate of termination with the first dose of lidocaine was 6 of 35 (17%; average dose 1.20 mg/kg). 29 patients failed initial lidocaine treatment and were treated with a second intervention: 23 received a second bolus of lidocaine, 4 were cardioverted, 2 with other medications. Lidocaine success rate was 4 of 22 (18%). The overall termination rate with lidocaine for patients who received 1 or 2 boluses was 10 of 34 (29%). Overall, cardioversion was successful in 16 of 18 attempts (89%). The average successful dose was 89 J. The 2 failures were at doses of 30 and 70 J. For those patients initially treated with a lidocaine, univariate analyses was performed to determine clinical factors associated with drug efficacy. History of prior MI was associated with failure to terminate VT (only 1/21 [4.8%] was cardioverted with the first lidocaine bolus). In comparison, in success rate in patients without a history of MI was 5 of 14 (36%; odds ratio 11 p = 0.06, 95% CI 0.96-3.51). Moreover, only 1 of 19 patients with a clinical history of CHF responded to the initial lidocaine bolus. Thus, the response rate was 5% (p = 0.07 vs. pts with no CHF). There was no correlation between measured EF or physical signs of pulmonary rales or peripheral edema, and response rate. The authors conclude that lidocaine has poor efficacy in terminating VT, particularly in patients with history of prior MI. Success rate following a second dose appears to be comparable to that for administering the first. There were no life-threatening adverse effects.
Arbitrarily considered opposing in light of the low success rate, but there is no evidence to support that lidocaine performs worst or better than placebo.
No comment about industry funding.


LOE 4, fair quality, supportive, E (Prolonged AAD treatment: amiodarone infusion)
Case series of 35 patients with life-threatening ventricular tachycardia (VT) refractory to conventional antiarrhythmic agents treated with high-dose IV loading regimen of amiodarone. All patients had been hospitalized for at least 1 day and VT was recurrent with a frequency of >1 episode per 2 h requiring on average 5.8 DC shocks. Amiodarone was administered as a loading dose of 5 mg/kg over 30 min followed by 20-30 mg/kg/day for 5 days. 22 of the 35 (63%) patients responded. Response from 0 to 2 h was seen in 7 (20%) patients, and 20 (57%) in the first 24 h. Of 13 non responders, 10 died secondary to lethal arrhythmia. Serious adverse events, requiring drug discontinuation or dosage reduction occurred in 13 (37%): hypotension in 8 (23%), symptomatic bradycardia in 4 (11%), sinus arrest lasting resulting in 20 min of bradycardia and hypotension in 1. Amiodarone plasma concentrations in patients with serious adverse events were not significantly different from the whole as a group. Minor side effects not requiring interruption of amiodarone administration occurred in 23 (66%) of patients. The authors conclude that despite the attempt to improve response rate through a high-dose loading regimen, amiodarone efficacy was comparable to that reported in the literature with lower doses; in addition serious toxicity was increased suggesting that 10-20 mg/kg/day for 3 days should be used.
No comment about industry funding.

Assumed LOE 4, fair quality, supportive, E (Prolonged AAD treatment: amiodarone infusion). Waiting full text from library


LOE 4, fair quality, supportive, C. Prospective evaluation on the efficacy of sympathetic blockade in treating patients with electrical storm (ES) and compared the outcome with that of patients with ES treated according to ACLS guidelines. The study included patients with recent MI and ES, defined as >= 20 VT/VF episodes per day or >= 4 VT/VF episodes per hour. After initial treatment according to the ACLS guidelines, 2 treatment approaches were used: patients in group 1 (n=27) received sympathetic blockade (6 with left stellate ganglion blockade, 7 with esmolol, and 14 with propranolol), patients in group 2 (n=22) continued to received conventional ACLS-guided therapy (lidocaine-procainamide-bretylium). After the initial acute sympathetic blockade treatment, patients who were able to take oral drugs were also given oral amiodarone. The two groups were similar with regard to clinical characteristics. All group 1 patients continued to have multiple VF episodes before sympathetic blockade (25+/−12). After sympathetic blockade therapy was initiated, the mean number of VF episodes was reduced to 2.6+/−1.7 in group 1 (P<0.01). In contrast, 91% of patients in group 2 continued to have VF episodes. At 1 week, 18 (82%) group 2 patients died, in contrast with only 6 (22%) patients in group 1. Survival to hospital discharge was of 20 patients in group 1 and only 2 in group 2. Important limitations: there was no randomization, assignment to treatment protocol was based only on physician preference; ACLS-guided therapy relied on old antiarrhythmic concepts according to the 1994 guidelines; the sympathetic blockade group received when possible concomitant therapy with oral amiodarone.

No comment about industry funding.


LOE 4, fair quality, supportive, E (Prolonged AAD treatment: amiodarone infusion). Retrospective review of medical records of patients receiving IV amiodarone for >= 1 episode of ventricular tachyarrhythmia requiring emergent therapy (e.g. DC shock) in the preceding 24h. Arrhythmias were divided in two groups: a) sustained unstable VT/VF associated with cardiovascular collapse; b) sustained symptomatic VT but without loss of consciousness. From April 1983 to March 1987 22 patients met selection criteria. Ventricular arrhythmias were refractory to 3.7+/−1.1 antiarrhythmic drug (AAD). Amiodarone was administered as initial bolus infusion of 200-480 mg, followed by continuous infusion of 900-1,600 mg/day. In the 24h before IV amiodarone patients: a) had 2.4+/−2.3 episodes/patient of life-threatening arrhythmias, b) required 4.0+/−3.9 DC shocks/patient, c) had 0.7+/−0.9 episodes/patient of sustained symptomatic VT. Within the first 24h of therapy patients: a) had 1.1+/−1.6 episodes/patient of life-threatening arrhythmias, b) required 1.9+/−3.1 DC shocks/patient, c) had 0.4+/−0.8 episodes/patient of sustained symptomatic VT. By 48h of amiodarone infusion patients: a) had 0.4+/−0.7 episodes/patient of life-threatening arrhythmias, b) required 0.4+/−0.9 DC shocks/patient, c) had 0.2+/−0.5 episodes/patient of sustained symptomatic VT. Overall the study reports a suppression of life-threatening arrhythmias in 50% and 64% of patients respectively within 24h and 48h. 19 of 22 patients continued for the first 24 h 1.6+/−1.0 AADs. There were no episodes of bradycardia, AV-block, or significant hypotension reported, not even following the initial bolus.

No comment about industry funding.


LOE 4, fair quality, neutral, E. A case series of patients treated with adenosine for tachycardia, including 24 with broad complex tachycardia. The study confirms the diagnostic utility of adenosine in revealing broad complex tachycardia of supraventricular origin (90% sensitivity, 93% specificity, and 92% predictive accuracy). Of notice symptomatic side effects were frequent (64%) and often severe (36%). No comment about industry funding.


LOE 4, fair quality, opposing, E (Acute termination). A case series based on retrospective review of records of 57 episodes of VT incorrectly diagnosed as supraventricular tachycardia and treated with IV verapamil. The dose ranged from 2.5 to 30 mg. A serious adverse response occurred in 42% (n=24/57): in 2 tachycardia accelerated with hemodynamic deterioration, in 22 hypotension occurred, 2 patients sustained cardiac arrest. Broad complex VT persisted in 79% of cases (n=45). No patient characteristic was predictive of the response to verapamil.

LOE 4, fair quality, supportive, E (Acute termination)
Prospective uncontrolled study on intramuscular self-injection of lidocaine (300 mg) in patients with documented ventricular tachyarrhythmias. In patients subscribing to SHALAL Medical Services between 1987 and 1995, the LidoPen injector was used in the following cases: transtelephonic electrocardiographic transmission of a sustained broad complex tachycardia suspected to be of ventricular origin, multiple polymorphic symptomatic ventricular premature beats associated with chest discomfort, and when time to arrival of a medical team was estimated to be >8 min. The population investigated had a history of previous myocardial infarction in 76% of cases, congestive heart failure in 36%, cardiac arrest and resuscitation in 17%. A total of 148 instructions to inject were provided over the telephone, 137 were successfully accomplished. Lidocaine self-injection resulted in conversion of 36% of cases in which sustained VT was recorded. Both responders and non-responders were similar except for a higher percentage of non-responders with a history of previous myocardial infarction and a lower mean systolic blood pressure. The main criticism is that, having no control, spontaneous cardioversion cannot be ruled out.


LOE 4, good quality, neutral E (Prolonged AAD treatment: amiodarone infusion)
Prospective randomized double-blind dose-range study designed to evaluate the efficacy and safety of IV amiodarone for patients with hemodynamically destabilizing VT or VF. Eligible patients had either incessant VT or hemodynamically destabilizing VT or at least two episodes of VT/VF within the last 24 h. They also had to be refractory to lidocaine, procainamide, and bretylium within the preceding 72 h. Treatment consisted in 3 regimens of IV amiodarone infusion for 48 h (125 mg/die, 500 mg/die, and 1000 mg/die). Open label supplementation of 150 mg amiodarone over 10 min was allowed at physician discretion. Primary endpoint was VT/VF event rate. Secondary endpoint was time to first hemodynamically destabilizing VT/VF event. A total of 342 patients were enrolled. There was no baseline differences among the treatment groups. The median event rates were 1.68, 0.96, and 0.48 events per 24 h for the 125-, 500-, 1000-mg dose groups, respectively, failing to achieve statistical difference (primary endpoint) but showing a trend toward statistical significance (p=0.67). Time to first event showed a statistical significant dose-related increase (p=0.05); there was a difference between first and third group, but not between first and second, and second and third. After 48 h, 26% of the patients in 1000-mg group remained arrhythmia free, compared with 16% of patients in the 125-mg. Finally more patients in the 125-mg group remained arrhythmia free compared with 16% of patients in the 125-mg. More patients in the 125-mg group required supplemental infusions for breakthrough VT/VF event (p=0.05), suggesting that the 125-mg dose was less effective than higher doses. The most common complication was hypotension (26%), without difference in incidence among groups. There was no dose-response relation in the increase of the QTc interval as well. Limitations: absence of placebo group which was deemed unethical by investigators (dose comparison was used to overcome the problem); open label amiodarone supplementation reduced the power of the study.
The study was partially supported by a grant from Wyeth-Ayerst Research.


LOE 4, fair quality, neutral E (Acute termination).
A case series (26 patients) on IV amiodarone as second line therapy for termination and short term control of recurrent sustained ventricular tachycardia (VT) and ventricular fibrillation (VF). Amiodarone was delivered as a 5 mg/kg short term infusion within 20 min, followed by continuous IV infusion (1050 mg/24h). In 19 of 26 patients were treated with the intent of terminating hemodynamically stable sustained VT. Amiodarone was successful in 8/19 (42%) within an average of 31 +/- 20 min (at 60 min electrical cardioversion was attempted). Because all patients were initially treated with other antiarrhythmic agents until just before the start of amiodarone, an addictive effect cannot be ruled out.
No comment about industry funding.


LOE 5, fair quality, supportive, E (Acute termination)
Classified as LOE5 because the study population does not correspond to that investigated by the worksheet. Overall the study suggests that nifekalant is more effective than lidocaine in prehospital VF/VT refractory to defibrillation. The amount of patients with VT was small.


LOE 1, poor quality, supportive, B E (Prolonged AAD treatment: amiodarone infusion).
A multicenter double-blinded, parallel-designed, randomized trial evaluating the effectiveness of amiodarone (Amio-Aqueous) and lidocaine on shock resistant VT (lidocaine intended as control). Patients had to be in incessant VT defined as sustained VT refractory to electrical shocks with a heart rate of >120 beats/min. It is not specified whether VT was mono or polymorphic. Initially, the patient received a bolus of either 150 mg amiodarone or 100 mg lidocaine administered over 2 minutes. If VT persisted, the patient received a second bolus. If VT did not terminate, the patient was electrically shocked. If VT terminated, the patient continued with a 24-hour infusion. If the patient failed to respond to the first assigned sequence, a crossover was allowed so the patient could receive the alternative sequence. The following end points were measured to evaluate efficacy: (1) termination of the VT, (2) survival at 1 hour, (3) survival at 24 hours (primary end point). Both groups had similar baseline characteristics. Approximately 50% of patients were hemodynamically unstable (10/18 amio vs 5/11 lido, p=ns). Amiodarone resulted in VT termination in 78% of the patients, whereas the success rate for lidocaine was 27% (p<0.05). At 1 hour after the initial bolus, 1 lidocaine patient was alive (9%) vs 12 (67%) randomized to amiodarone (p<0.01). At 24 hours 1 (9%) and 7 (39%) patients respectively were alive (p<0.01). In the amiodarone group, there were no statistically significant differences between hemodynamically stable and unstable patients in the rate of VT termination (stable 73%, unstable 80%), 1-hour survival (stable 75%, unstable 60%), and in 24-hour survival (stable 38%, unstable 40%). The only patient who completed the 24-hour study in the lidocaine group was hemodynamically stable before receiving lidocaine. The incidence of hypotension was 7% for amiodarone and 28% for lidocaine (p=0.06). In conclusion, Amio-Aqueous, a water soluble intravenous amiodarone preparation, is more effective than lidocaine for the termination of shock-resistant VT and in terms of survival. Limitations: low number of patients enrolled (11 vs 18). The study was prematurely discontinued due to amiodarone superiority after interim analysis.
Sponsored by Academic Pharmaceuticals, Lake Bluff, Illinois.


LOE 4, fair quality, opposing, E (Acute termination).
Case series based on retrospective review of 1 year of patients with wide complex VT. No details as to wethere VT was mono or polymorphic is provided, but all available figures show monomorphic VT samples. Out of 38 episodes, 15 were misdiagnosed as supraventricular tachycardia, therefore receiving inappropriate therapy with consequent unfavorable outcome compared to those with adequate treatment (p<0.01). In 13 out of 15 episodes (87%) misdiagnosed the patient condition worsened (compared to 4/23 correctly diagnosed and appropriately treated): hypotension occurred in all, tachycardia accelerated in 2, VT degenerated in VF in 2. In all 13 episodes patients were treated with verapamil, the remaining 2 although misdiagnosed did not receive verapamil and did not worsen.
Supported in part by a grant from the American Heart Association, Washington Affiliate, and the Seattle Medic I Emergency Medical Services Foundation.


LOE4, fair quality, neutral, E (Acute termination).
A cases series of retrospectively identified patients with hemodynamically-tolerated sustained (>15 min) monomorphic VT hospitalized between March 2003 and October 2006. Intervention: 300 mg of amiodarone administered IV over 30 min. Endpoints: a) VT termination within 20 min and 1 h of start of drug administration, b) rate of cardioversion necessary within 1 h due to hemodynamic deterioration. Patients identified were 41, most (85%) with ischemic heart disease (mean LVEF 0.31). VT terminated in 20 min in 6/41 (15%) and within 1 h in 12/41 (29%). There were no deaths during amiodarone infusion. Symptomatic hypotension requiring electrical therapy occurred in 7/41 (17%, mean time to cardioversion 42 min).
No funding declared.


LOE 4, fair quality, neutral, E (Acute termination)
A policy for emergency unit staff recommending the management of acute sustained symptomatic tachyarrhythmias by electrical cardioversion as first line therapy instead of antiarrhythmic agents was instituted. Data was prospectively acquired to determine the efficacy and safety of such strategy when adopted by non-cardiological junior staff. In 16 month 52 tachyarrhythmic events were treated, including 7 patients presenting with sustained VT. Of 52 episodes 10 responded to vagal maneuvers, leaving 43 patients treated with electrical cardioversion. Synchronized shocks were successful in 98% (42/43), and in all patients with VT (7/7). No complications reported, including the sedation procedure-

Wang JC, Lim SH, Teo WS, et al. (2002). "Calcium channel blockers as first line treatment for broad complex tachycardia with right bundle branch block: ingenuity or folly?". Resuscitation 52: 175-82.

LOE 4, fair quality, supportive, E (Acute termination).

Case series of retrospective chart review of patients presenting at the ED with broad complex tachycardia and right bundle branch block, but without evidence of ischaemic heart disease between 1992 and 1998. 25 patients fulfilled the eligibility criteria for review. All but 1 patient (18/19, 95%) treated with calcium channel blockers (verapamil/diltiazem) were successfully cardioverted. When IV adenosine (3), lidocaine (2) or amiodarone (1) were used as first line treatments, none of the patients were converted to sinus rhythm. One patient, who was given lidocaine (50 mg IV) followed by verapamil (5 mg IV), deteriorated hemodynamically and required 200J of synchronised DC cardioversion. Although the incidence of broad complex tachycardia plus RBBB is relatively rare (35 instances in 6 years), respond well to calcium channel blockers given as the first drug of administration, provided that they have a negative history for ischemic heart disease. This can be considered a specific clinical entity that comprises idiopathic left ventricular tachycardia.


LOE 3, good quality, supporting, E (Prolonged AAD treatment: nifekalant bolus + infusion)

This study examined the use of nifekalant in patients with sustained VT or VF. About 60% of the patients had VT. The study compared nifekalant to lidocaine (historical control).


LOE 5, good quality, neutral, review.

Guidelines with treatment recommendations on ventricular arrhythmias including ventricular tachycardia (VT). Specific sections address the following conditions relevant to the WS question: unstable sustained VT associated with acute coronary syndromes, VT associated with low troponin myocardial infarction, sustained monomorphic VT, repetitive monomorphic VT.