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

**Worksheet author(s)**

<table>
<thead>
<tr>
<th>MD, PhD Markus Skrifvars</th>
<th>Date Submitted for review: First submission July 9th, 2008</th>
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<tbody>
<tr>
<td>Based on the 2005 worksheet of MD Hans Domanovits</td>
<td>Second submission November 11th, 2008</td>
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<td>Third submission February 19th, 2009</td>
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<td>Fourth submission July 22nd, 2009</td>
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<td>Fifth submission September 1st, 2009</td>
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<td>Webinar presentation November 12th, 2009</td>
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<td>Sixth submission December 15th, 2009</td>
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<td>Seventh submission January 7th, 2010</td>
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**Clinical question.**

"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/therapy

State if this is a proposed new topic or revision of existing worksheet: This is a revision of an existing worksheet

**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).**

This current worksheet is an update of the worksheet of MD Hans Domanovits from 2005. The studies included in the previous review of MD Hans Domanovits will be reevaluated for inclusion and for updating the grading of level of evidence due to the different grading system to be used in the 2010 Guidelines. In addition to this, new literature searches will be performed to find studies published after the previous worksheet and in order to find any studies left out from the 2005 worksheet.

The worksheet process can therefore be divided into two parts:

1. Reevaluate the studies in the worksheet of 2005 taking into account inclusion criteria and the modified way of grading evidence. Include studies if none of the exclusion criteria exist and if the study population is equivalent.

2. Perform new searches in order to find relevant articles published after July 6th, 2004 and any other possible articles not included in the previous worksheet.

Searched databases: AHA Endnote 7 Master Library, PubMed, Cochrane Database for Systematic Reviews

The appropriate Medical Subject Headings (MeSH) were identified for key-words used by MD Hans Domanovits from 2005, i.e. “ventricular tachycardia” AND “drug therapy” AND “treatment outcome”. An effort was made to exclude some studies according to the exclusion criteria using a limited search, mainly for excluding animal studies and pediatric studies.

Manual search for relevant references included in any possible review articles or Task Force Reports identified in the searches performed.

- State inclusion and exclusion criteria
Exclusion criteria:

1. Studies on children
2. Prevention of VT using oral medications
3. Pulseless VT mandating chest compressions or immediate cardioversion.
4. Animal studies
5. Studies were VT is induced during an electrophysiological study (i.e. cath lab)
6. Studies with the abstract in languages other than English, German, Swedish or Finnish
7. Polymorphic ventricular tachycardia or torsades de pointes
8. Case reports
9. Study on other issue than the posed research question

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

Evaluation of studies in the worksheet of 2005

1) The 19 studies of the worksheet of 2005 were reviewed:

a) Three studies (Keren et. al. 1981, Tzivoni D et al. 1988, Credner et al. 1998) were excluded because the study populations were polymorphous VT (Torsades de Pointes) or patients with electrical storm. The “clinical question” of the worksheet specified “monomorphic tachycardia.

b) All included studies were reevaluated in order to grade the evidence in accordance with requirements of the 2010 worksheets (Level of evidence 1-5 and quality good, fair or poor).

The following changes were made:

I. The study by Koster et al. NEJM 1985 is an excellent study (a randomized controlled trial) but the population was patients with acute myocardial infarction, in the pre-hospital setting, and lidocaine was administered prophylactically in order to prevent the occurrence of arrhythmias. Apparently some of the patients had or eventually got ventricular tachycardia, and in these patients (14 patients all in all), intramuscular lidocaine was efficient. However since the original study population is different to that of the clinical question, therefore study is labeled LOE 5 of good quality (as opposed to LOE1, fair quality in the 2005 worksheet).

II. The study by Chevalier et al. International Journal of Cardiology 1998 is labeled LOE 4, fair quality in the present worksheet. The study is a case series but the population is the one of the “clinical question”.

III. The study by Domanovits et al. Resuscitation 1999 is labeled as neutral to the clinical question since 50% of the patients with stable VT converted to sinus rhythm and the rest required electrical cardioversion. The study is labeled LOE4, fair quality.

IV. The study Marill et al. Acad Emerg Med 1997 was labeled LOE4, poor quality (LOE5 in 2005).


VI. The study by Rankin et al. Lancet 1987 was labeled LOE4, poor quality (LOE5 in 2005).

VII. The study by Stewart et al. Ann Intern Med 1986 was labeled LOE4, poor quality (LOE5 in 2005).
VIII. The study by Manz et al. New Trends in Arrhythmias 1991 was designated as a trial supporting the use of magnesium in stable monomorphic VT, LOE 4.

New searches performed for the present worksheet

The appropriate MeSH keywords were identified. The following were found and used; "Tachycardia, Ventricular"[Mesh], "drug therapy"[Subheading] and "Treatment Outcome" [Mesh].

2) A search of PubMed with Search "Tachycardia, Ventricular"[Mesh] AND "drug therapy"[Subheading] AND "Treatment Outcome" [Mesh]) limited to: Humans and All Adult: 19+ years

This search resulted in 162 articles that were reviewed for inclusion.

The following articles were found and were included in the worksheet;


Yield 1: 419 articles. Using an advanced search option studies with exclusion criterias 1 (studies on children), 4 (animal studies), 6 (studies on other languages than English, German, Swedish or Finnish) and 8 (case reports) were excluded and this resulted in 45 articles that were subjected for further review. (Limits: Humans, Clinical Trial, Editorial, Letter, Meta-Analysis, Practice Guideline, Randomized Controlled Trial, Review, Clinical Conference, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Comment, English, French, German, Finnish, Swedish, Core clinical journals, All Adult: 19+ years)

Yield 2: 61 articles. A further review of these resulted in including the following articles (apart from those already included based the worksheet from 2005 or from the previous search):


4) A search of references of review articles identified in the search above revealed the following additional studies;


5) A search of the Cochrane Library was performed on February 15th, 2009. The term “tachycardia, ventricular (MeSH)” was used. The search revealed; 0 Cochrane reviews, 6 other reviews and 403 clinical trials. These clinical trials were reviewed in order to find relevant articles. The following additional study was found:


This study seemed to be identical to the study Manz et al. 1991 that is already included in the worksheet, therefore this (Manz et al. 1997) study will not be included. Interestingly the results are similar but the conclusion is different, the former study recommends the use of magnesium and the latter does not.

6) A search of the EMBASE database was performed. This did not reveal any additional studies.

7) A redo search of PubMed search was performed in August 2009. Two new studies were found. In addition it was decided to include two studie on the use of nifekalant, a new drug mainly used in Japan.


8) A search of previous international guidelines on treatment of ventricular arrhythmias was performed. The following guidelines were identified:

a) The ACC/AHA/ESC guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac arrest from 2006. One study on the use of procainamide and one on immediate cardioversion in VT were found and were included.


Therefore all in all 32 studies were included in the present worksheet.

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Summary of evidence

Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Ho 1994 E, sot</th>
<th>Katoh E, C, nifek</th>
<th>Koster 1985 E, lid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Somberg 2002 E, B24, E, amio /lido</td>
<td>Schmidt 1988 E, amio</td>
<td>Shiga 2009 E, nifek, lido</td>
</tr>
<tr>
<td></td>
<td>Ando 2005 E, C, nifek, lido</td>
<td>Schutzenberger 1989 E, amio</td>
<td>Roth 1997 E, lid</td>
</tr>
<tr>
<td>Level of evidence</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>-------------------</td>
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<td>---</td>
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</tr>
<tr>
<td>Poor</td>
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</tbody>
</table>

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

### Evidence Neutral to Clinical Question

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<tbody>
<tr>
<td>Fair</td>
<td>Manz 1991 E, Mg</td>
<td>Mooss 1990 E, amio</td>
<td>Ando 2005 E, nifek, lido</td>
<td>van der Watt 1995 E, cardiov</td>
</tr>
<tr>
<td>Poor</td>
<td>Klein 1988 E, amio</td>
<td></td>
<td></td>
<td>Sharma 1990 E, proca</td>
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</tbody>
</table>

### Evidence Opposing Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th>Marill 2006 E, amio</th>
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<tbody>
<tr>
<td>Fair</td>
<td>Armengol 1989 E, lido</td>
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<tr>
<td></td>
<td>Stewart 1986 E, vera</td>
</tr>
<tr>
<td></td>
<td>Nasir 1994 E, lido</td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
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</table>

**Level of evidence**

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

*Italics = Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Stable ventricular tachycardia is a rather uncommon but potentially serious condition given the risk of conversion to ventricular fibrillation and subsequent cardiac arrest (DeSanctis, 1965, 96). Cardioversion is efficacious in most cases and is therefore a reasonable treatment option at any stage (van der Watt, 1995, 508). However it requires sedation and therefore when unavailable drug treatment can be considered first line treatment (DeSanctis, 1965, 96). The 2005 guidelines suggested using amiodarone, procainamide or sotalol without preferring any medication over the other (American Hearts Association Guidelines 2005, 2005, 25).

The present worksheet is in essence an update of the worksheet of MD Hans Domanovits. There were only three recent studies published since the completion of MD Hans Domanovits worksheet that were included (Tomlison, 2008, 15; Marill, 2006, 217; Marill, 2009, 2512). In addition the level of evidence of the included studies had to be reevaluated because of a different grading system in the 2010 worksheet.

Overall the quality of the retrieved studies according to the level of evidence was poor: there were three studies with level of evidence 1 and one with 3. All the other studies were level of evidence 4 or 5. Also the quality of evidence of all studies did not exceed “fair” except in one article. There were studies which report on use of antiarrhythmic drugs in patients with sustained VT which are available only in certain countries (Cibenzoline – available in France). Although comparable in the efficacy with drugs which are available in most countries, little is known about the importance of these drugs.

All in all the data suggests that drugs such as amiodarone and lidocaine seem to be are rather ineffective in terminating ventricular tachycardia (Tomlison, 2008, 15; Marill, 2006; Armegol, 1989, 254; Nasir, 1994, 1183; Marill, 1997, 1122). Amiodarone seems to be associated with side-effects the effects of which on outcome is however not clear (Mooss, 1990, 691; Schutzenberger, 1989, 367; Tomlison, 2008, 15; Marill, 2006, 217). **Amiodarone seems to be the most studies drug for VT and probably the most widely used (Mooss, 1990, 691; Schutzenberger, 1989, 367; Tomlison, 2008, 15; Marill, 2006, 217).**

Higher termination rates have been reported with the use of sotalol and procaiamide but few studies are available on their use, and it is unclear to what extent these drugs are in clinical use worldwide (Ho, 1994, 18; Gorgels, 1996, 43). Another new drug is nifekalant, a potassium channel blocker classified as a class three agent according to the Vaughan Williams Classification. Nifekalant has been developed in Japan and is currently only available there. The studies on the use of nifekalant seem very promising but side effects such as QT prolongation and torsades de pointes VT is possible.

Acknowledgements:
Included studies (in alphabetical order)


Department of Cardiology, Kokura Memorial Hospital, Kitakyushu, Fukuoka 802-8555, Japan.

Supporting
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. The study labeled LOE3 of fair quality.


Department of Medicine, Evanston Hospital, Northwestern University Medical School, Illinois 60201.

Opposing clinical question. Lidocaine given in up to three intravenous boluses totaling 75 to 400mg will terminate ventricular tachycardia in less than 20% based on a LOE4 study. Quality of evidence - fair.


Hôpital cardiovasculaire et pneumologique, Lyon-Montchat, France

Supporting
Intravenous cibenzoline in a dose of 70 + 12 mg may be useful in terminating spontaneous ventricular tachycardia. based on a LOE 4 study, quality of evidence - fair.


Department of Emergency Medicine, Vienna General Hospital, University of Vienna, Medical School, Austria. hans.domanovits@akh-wien.ac.at
Neutral, opposing
Intravenous administration of Class I (Lidocain) and Class III antiarrhythmic drugs may be useful to terminate stable sustained ventricular tachycardia based on a LOE 5 study. Quality of evidence - fair.


Department of Cardiology, Academic Hospital Maastricht, The Netherlands.

Supporting
Procainamide is superior to lidocaine in terminating spontaneously occurring ventricular tachycardia based on a LOE 1 study. Quality of evidence - fair.


Department of Medicine, University of California, San Francisco 94143-0214.

Supporting
Intravenous amiodarone is effective in patients with recurrent ventricular tachycardia or ventricular fibrillation refractory to other drugs based on a LOE 4 study. Quality of evidence - fair.


Neutral, opposing
Verapamil will rarely terminate ventricular tachycardia, however may cause transient hypotension based on a LOE 5 study. Quality of evidence – fair.


Department of Cardiology, Westmead Hospital, Sydney, NSW, Australia.

Supporting
Sotalol is significantly more effective for the acute termination of sustained VT than lidocaine based on a LOE 1 study. Quality of evidence - good.
Jenn CW, Swee HL, Wee ST, Anantharaman V. Calcium channel blockers as first line treatment for broad complex tachycardia with right bundle branch block: Ingenuity or folly? RESUSCITATION. Resuscitation 2002;52(2):175-182.

Supporting

Calcium channel blockers may be used in patients presenting with broad complex tachycardia and right bundle branch block but without underlying ischaemic heart disease based on this LOE 4 study.


Supporting

The main conclusion of this LOE4 study of good duality is that nifekalant does not seem to very effective in immediate conversion of a VT but seems to prevent re-occurrence.


Veterans Administration Medical Center, Albuquerque, NM 87108.

Neutral to the question whether amiodarone improves termination rates in VT.

This case series suggests that amiodarone suppressed VT in about 50% of the patients but recurrence was common. This study was labeled LOE4, quality poor.


Department of Cardiology, Academic Medical Center, Amsterdam, The Netherlands.

Supporting

Intramuscular lidocain 400 mg may terminate ventricular tachycardia in patients with acute myocardial infarction based on a LOE1 study. However in the present study lidocaine was administered to all AMI patients in the pre-hospital setting, only a few patients (14) were in VT. In addition for safety reasons (bleeding, hematoma) intramuscular administration of drugs during acute myocardial infarction is contraindicated. Therefore the level of evidence is 5, good quality.

Lankenau Hospital and Medical Research Center, Wynnewood, PA 19096, USA.

Neutral to question whether amiodarone or bretylium is better in the treatment of VT

This is a RCT trial comparing the use of amiodarone and bretylium in patients with recurring ventricular tachycardia or ventricular fibrillation, thus in most cases it was administered as a prophylactic. In 34 patients all in all (9 patients were given bretylium and 25 amiodarone of either high or low dose) had ventricular tachycardia at the time of administration. There was no difference in the termination rates between the drugs, although the study suffered from lack of power for this research question. This study is labeled LOE5 of good quality.


Arrhythmia Service, St. Francis Hospital, Roslyn, New York 11576, USA.

Neutral to the question whether amiodarone is efficient in VT patients.

In this study patients with refractory ventricular tachycardia not responding to lidocaine, procainamide or bretylium were randomized to one of three doses of amiodarone to be administered over 24 hours. There was no difference in the success rates between the groups. The study does not report whether the patients had ongoing VT at time of treatment. The response rate to amiodarone was around 40%. All in all the conclusion was that amiodarone seemed safe in these patients but not very effective. The study is labeled LOE4 of good quality.


Department of Cardiology, University of Bonn, Germany.

Supporting
Magnesium glutamate as a 2000 mg intravenous bolus can be considered as short-term intervention to control hemodynamically stable monomorphic ventricular tachycardia based on a LOE 4 study, quality of evidence - fair.

Texas Tech University, Department of Emergency Medicine, El Paso 79905-2060, USA. emmekam@ttuhsc.edu

Opposing
The potential of lidocaine for termination of spontaneous sustained stable ventricular tachycardia is low, particularly in patients with a history of myocardial infarction based on a LOE 4 study, quality of evidence - fair.


Massachusetts General Hospital, Boston, MA 02114, USA. kmarill@partners.org

Opposing
The case series suggests that amiodarone is not very effective in terminating monomorphic VT in the emergency setting. The study is labeled LOE4, fair quality.


Department of Emergency Medicine (KAM), Massachusetts General Hospital, Boston, MA, USA. kmarill@partners.org

Neutral
This case series examines the use of adenosine in diagnosing and treating wide complex tachycardias. The study suggests that adenosine may be used in diagnosing wide complex tachycardias. If the wide complex tachycardia is of ventricular origin it is unlikely to be terminated but on the other hand not associated with significant side effects according to this LOE4 study of good quality.


Creighton University Cardiac Center, Omaha, Nebraska 68131.

This study is neutral to the use amiodarone in VT
This case series examined the use of intravenous amiodarone for patients with VT. The majority of patients responded but there were a high incidence of side effects such as hypotension and
bradycardia so therefore no conclusion about the use of amiodarone can be made. This study I labeled LOE4, fair quality.


Cardiac Electrophysiology Unit, Methodist Hospital, Houston, Texas 77030.

Opposing the use of lidocaine in VT
A study of patients with either spontaneous or induced ventricular tachycardia treated with intravenous lidocaine. The termination rate was very low at only 8%. The study was labeled LOE 4 of fair quality.


Minneapolis Heart Institute, Minnesota 55407.

This study supports the use of amiodarone in patients with VT.
This case series examined the use of amiodarone in patients with VT. However it is unclear how many of the patients were in VT at the time of administration, therefore the study is labeled LOE5, fair quality.


University Department of Medical Cardiology, Royal Infirmary, Glasgow.

Neutral, opposing
Adenosine may be used for diagnosing the type of tachycardia in cases with a broad complex. However it will not terminate a ventricular tachycardia based on a LOE 5 study, quality of evidence - fair.


University Department of Medical Cardiology, Royal Infirmary, Glasgow.
Opposing
Verapamil is ineffective and potentially hazardous in most patients with ventricular tachycardia based on a LOE4 study, quality of evidence - fair.


Department of Cardiology, Tel-Aviv Sourasky Medical Center, Israel.

Supporting the use of intramuscular lidocaine in patients with VT.

This study reports the use of self-administered intramuscular lidocaine in the pre-hospital setting. Of the patients with a documented rapid ventricular tachycardia and that were given lidocaine 35% had sinus rhythm restored. The study is labeled LOE4, fair quality.


Department of Cardiology, University of Ulm, West Germany.

Suggests that amiodarone is efficient in terminating VT
In this retrospective case series amiodarone was found to be efficient in treating VT. The study is LOE4 of fair quality.


Medizinische Abteilung des Allgemeinen Krankenhauses, Stadt Linz, Austria.

Supporting
Intravenous amiodarone may terminate spontaneous sustained ventricular tachycardia in patients with organic heart disease accompanied by depressed left ventricular function based on a LOE 4 study, quality of evidence - fair.


Mercy General Hospital, Sacramento, Canada.
Neutral
Intravenous procainamide can cause significant hemodynamic compromise in some patients with ventricular tachycardia. This study is labeled LOE 5 of fair quality.


Supporting
This LOE5 study of fair quality suggests that nifekalant is more effective than lidocaine in prehospital VF/VT refractory to defibrillation. The amount of patients with VT was small.


Rush University, Chicago, Illinois, USA

Supporting
A new aqueous formulation of amiodarone is more effective than lidocaine in the treatment of shock-resistant VT based on a LOE 1 study, quality of evidence fair.


Opposing
Verapamil given in patients with misdiagnosed VT is frequently associated with poor outcome based on a LOE4 study, quality of evidence – fair


Department of Cardiac Rhythm Management, John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, UK.

Opposing
The case series suggests that amiodarone is not very effective in terminating monomorphic VT in the emergency setting. The study is labeled LOE4, fair quality.


Department of Medicine, University of Cape Town.


The Second Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan.

Supporting
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) and was therefore labeled as LOE3 of good quality.