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

**Worksheet author(s)**

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**Clinical question.**

“In patients with suspected ACS/MI in prehospital and emergency department setting, does the use of prophylactic antiarrhythmics compared with standard management (i.e., no prophylactic antiarrhythmics), improve outcome (e.g., arrhythmias, survival to discharge, 30/60 d mortality)?”

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

**State if this is a proposed new topic or revision of existing worksheet:** New

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**Conflict of interest specific to this question**

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

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

PubMed – ((acute coronary syndrome) or (myocardial infarction)) and (arrhythmia, cardiac) and (clinical trial) and ((lidocaine) or (adrenergic beta-antagonists)) initially; focused only on lidocaine after noting that it is not possible to separate out the antiarrhythmic effects of beta blockers from their effect on myocardial supply:demand in an acute coronary syndrome.

EMBASE – (acute coronary syndrome or myocardial infarction) and (lidocaine)

Cochrane – 21 articles found (1 relevant, duplicate of PubMed search)

AHA Endnote Master Library; Cochrane database for systemic reviews, review of references from articles

Forward search using SCOPUS and Google Scholar.

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**State inclusion and exclusion criteria**

Inclusion - studies evaluating use of prophylactic use of lidocaine, tocainide and disopyramide in acute coronary syndromes (including STEMI, NSTEMI, U/A). Given the large number of meta-analyses performed on the lidocaine RCTs, the meta-analyses and not the individual RCTs were included in the worksheet.

Exclusion – studies evaluating antiarrhythmic drugs other than lidocaine tocainide and disopyramide (e.g. beta-blockers); abstract only studies.

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

PubMed – 94 lidocaine articles (included 6 metanalyses)

EMBASE – 1/28 articles pertinent (duplicates of PubMed search)

Cochrane – 0/4 Cochrane reviews; 0/1 other reviews; 1/15 clinical trials (duplicates of PubMed search)

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# Summary of evidence

## Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Fair**          | DeSilva, 1981, 855  
|(Lido: E)*        |      |      |      |
| MacMahon, 1988, 1910  
|(Lido: E)*       |      |      |      |
| Sadowski, 1999, 792  
|(Lido: E)        |      |      |      |
| Teo, 1993, 1589  
|(C: Amiodarone, Betablockers)* |      |      |      |
| **Poor**          |      |      |      |

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</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 (VF incidence)  

*Study combines results of other studies.  
Lido = Lidocaine  
*Italics = Animal studies
### Evidence Neutral to Clinical question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hine, 1989, 2694 (Lido: C; pre-hospital RCTs)*</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>MacMahon, 1988, 1910 (Lido: C)*</td>
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<tr>
<td></td>
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<td>Sadowski, 1999, 792 (Lido: C)</td>
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<td>Sadowski, 1999, 792 (Lido: C, E)*</td>
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<tr>
<td></td>
<td></td>
<td>Teo, 1993, 1589 (C: Ca channel blockers)*</td>
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</tr>
</tbody>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
C = Survival to hospital discharge  
E = Other endpoint (VF incidence)  
B = Survival of event  
D = Intact neurological survival  
*Study combines results of other studies.

### Evidence Opposing Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hine, 1989, 2694 (Lido: C, hospital phase RCTs)*</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Teo, 1993, 1589 (C: Class 1 agents)*</td>
<td></td>
</tr>
</tbody>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
C = Survival to hospital discharge  
E = Other endpoint (VF incidence)  
B = Survival of event  
D = Intact neurological survival  
*Study combines results of other studies.

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

REVIEWER FINAL COMMENTS: Only prophylactic lidocaine can be assessed adequately based on the lack of trials on other agents (although there are data on beta blocker or amiodarone use, it is not clear whether any effects are due to the potential antiarrhythmic properties of beta blockers or amiodarone vs. their effects on myocardial supply:demand). There are 6 publications in the literature that have pooled data from smaller trials into larger metanalyses (see below table).

<table>
<thead>
<tr>
<th></th>
<th>DeSilva et al., 1981</th>
<th>MacMahon et al., 1988</th>
<th>Hine et al., 1989</th>
<th>Teo et al., 1993</th>
<th>Sadowski et al., 1999</th>
<th>Alexander et al., 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td># trials included</td>
<td>15</td>
<td>14</td>
<td>14</td>
<td>17</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>VF prevalence</td>
<td>Lower with lido</td>
<td>Lower with lido</td>
<td></td>
<td></td>
<td>No difference (trend towards lower with lido)</td>
<td>No difference</td>
</tr>
<tr>
<td>Mortality effect</td>
<td>Not reported</td>
<td>No difference (trend toward higher mortality with lido)</td>
<td>Worse for lidocaine given in-hospital</td>
<td>No difference (trend toward higher mortality with IV lido)</td>
<td>No difference (trend toward higher mortality with lido)</td>
<td>No difference</td>
</tr>
</tbody>
</table>

These are the only studies that are being classified on the template because all other reports are too small in size to reach any statistically significant conclusions, and those that have even fair quality are included in the reported metanalyses.

There are major confounders with this evidence analyses, including:

1. Most of the prophylactic lidocaine studies used different dosages, dosing regiments, routes (IV vs. IM), sites of administration (prehospital vs. in-hospital)
2. Most of the studies were prior to fibrinolytic use; virtually all prior to PCI use
3. Most of the studies from 1970s and 1980s were underpowered and of poor design (many without proper randomization)
4. VF only occurs in a small % of MI patients, only 1 of 6 cases prove fatal in hospital
5. Most early studies only report short-term follow-up results
6. Early studies did not have modern diagnostic tests – metanalyses exclude at least 8% of patients because the diagnosis of acute MI could not be confirmed in the study population
7. Use of prophylactic lidocaine has decreased markedly since the advent of fibrinolysis (down to 3.5% in 1990) and the ACC/AHA Guidelines published in 1990 and subsequently based on metanalyses done in the late-1980s; thus, there are no “modern” studies to evaluate and the question is essentially of historical interest only.

### Acknowledgements:

None.
Citation List

ARTICLES DISCUSSED/INCLUDED IN WORKSHEET:


Comment:
LOE 2, Fair. Supportive for 24 hour survival, but neutral for hospital discharge. Combination of data from 2 RCTs, although randomization was not for lidocaine and pts treated with fibrinolysis, not PCI. Only study in the modern reperfusion era.


Comments:
LOE 1, Fair, Neutral. Compared tocainide and disopyramide and placebo. No difference between groups for VF or deaths. Both tocainide and disopyramide decreased ventricular premature beats.


Comment:
LOE 1, Fair, Supportive of decrease in VF. Meta-analysis of 15 RCTs of lignocaine treatment to prevent VF. Earliest attempt at a combined analysis of multiple small trials. No mortality data reported.


Comments:
LOE 1 (meta-analysis of RCTs), Fair, opposing (for mortality, hospital phase RCTs), neutral (prehospital-phase RCTs),


Comment:
LOE 1 ("over-view of 14 RCTs"), Fair, Supportive (VF), and neutral (early [24-48 hr] mortality). First “metanalysis” to show no statistically significant difference in mortality with use of prophylactic lidocaine (trend for higher mortality with lidocaine).


Comment:
LOE 1 (RCT and meta-analysis of RCTs), Fair, Supportive (for VF in RCT), Neutral (for VF in meta-analysis, and mortality in RCT and meta-analysis).


Comment:
LOE 1 (meta-analysis or RCTs and parallel trials), Supportive (mortality better for beta-blockers and amiodarone), Neutral (mortality for Ca Channel blockers), Opposing (mortality worse for Class 1 agents).

OTHER ARTICLES FROM SEARCH BUT EXCLUDED FROM DISCUSSION/INCLUSION IN WORKSHEET:


Comment - although not a randomized trial, documents the decreasing prevalence of VF and its implications to the use of prophylactic lidocaine.


