Maine Medical Center  
Department of Emergency Medicine  

Journal Club / Research Article Summary - (Adapted from Schultz Table)  

Date:  1/15/2013  
Presenter: Jordan Maresh  

ARTICLE:  
- Paul Dorian is a professor of Pharmacology and director of the Division of Cardiology at the University of Toronto  
- **Country:** Toronto, Ontario  
- **Funding Sources:** Wyeth-Ayerst Laboratories [now Wyeth Pharmaceuticals]  
  - Unrestricted research grant, however, “the investigator-initiated protocol was designed, drafted, and executed, and the results were analyzed without any contribution from the study sponsors”  
  - Makers of products such as Advil, Robitussin, ChapStick, and Preparation H.  
  - Provided the drug-administration kits used in the study  

PURPOSE:  
- **Research Question(s):** How does amiodarone compare to lidocaine for treatment of shock-resistant out-of-hospital ventricular fibrillation?  
- **Hypothesis:** Not explicitly stated, but the trial was powered to show superiority of amiodarone to lidocaine with a goal increase in survival to admission from 25% to 40%.  

DESIGN:  
- **Study Design:** Prospective, randomized, double blind, placebo-controlled trial  
- **Outcomes:**  
  - Primary – Survival to hospital admission  
  - Secondary –  
    1. Survival to hospital discharge  
    2. Adverse events defined as administration of atropine or dopamine after study drug-administration  

SETTING / SUBJECTS:  
- **Research Setting:**  
  - November 1995 to April 2001
○ Toronto Emergency Medical Services (multi-tiered out of hospital emergency response system)
○ Patients were admitted to one of 17 community hospitals without disclosure of medication given or further research driven instructions for treatment

• Subjects:
  ○ Number of Studies / Subjects:
    347 total patients (mean age 67±14 years)
    180 to amiodarone group
    167 to lidocaine group
  ○ Inclusion / Exclusion criteria:
    Inclusion
    – ECG evidence of VF or other rhythms that converted to VF
    – VF resistant to three shocks from defibrillator, 1+ dose of IV epinephrine and a fourth shock (in accordance with 2000 AHA treatment protocol for advanced cardiac life support)
    – includes patients with recurrent VF after initial successful defibrillation
    Exclusion
    – Trauma
  ○ Demographics:
    Amiodarone group:
    76% male, 68±14 years, 61% history of cardiac disease, 76% witnessed arrest, 26% CPR by bystander
    Lidocaine group:
    81% male, 66±13 years, 59% history of cardiac disease, 78% witnessed arrest, 28% CPR by bystander

Dispatch to Drug Administration was near equivalent between groups with 25±8 minutes for amiodarone and 24±7 for the lidocaine group.

METHODS:
• Interventions:
  ○ After the initial shocks and epinephrine patients received either:
    1. Amiodarone 5 mg/kg estimated body weight and lidocaine placebo OR
    2. Lidocaine 1.5 mg/kg with amiodarone placebo
  ○ If patients had persistent VF after study drug administration and another shock they received
    1. Amiodarone 2.5 mg/kg or Lidocaine 1.5 mg/kg each with placebo
• Data was analyzed prior to revealing study groups
Data was obtained from the ambulance call report, from the dispatch center and from hospital charts.

DATA ANALYSIS:

Statistics Used:
1. Sample size calculation to show estimated improvement in survival to admission from 25% to 40% between lidocaine and amiodarone groups.
2. Continuous Variables
   - Wilcoxon rank-sum testing to compare groups
   - Means, standard deviations, and medians
3. Categorical Data
   - Summarized as frequencies and percentages
   - Comparison performed by Pearson chi-square test or Fisher's exact test
4. Multiple logistic regression with backward selection of variables and calculation of odds ratio to identify predictive variables for primary outcome.

RESULTS:

Brief answers to research questions:
- Survival to Admission: Of 180 patients in the amiodarone group, 41 patients, or 22%, survived to admission compared to 20 patients, or 12%, of 167 patients in the lidocaine group.
- Survival to Discharge: Nine amiodarone group patients survived to discharge, while five of the lidocaine group patients survived to discharge. This difference was not statistically significant (p = 0.34).
- Usage of dopamine or atropine between groups was not significantly different.

Table 2: Odds ratios for survival to hospital admission according to selected factors
- Treatment assignment (amiodarone vs. lidocaine): 2.49 (1.28-4.85) p = 0.007
- Time from dispatch to drug administration (per 1 min increase): 0.88 (0.83-0.93) p < 0.001
- Transient return of spontaneous circulation before drug administration: 5.93 (2.46-14.26) p < 0.001
- Note: amiodarone group had more patients with transient ROSC than lidocaine group (24 compared to 11 patients).

IMPLICATIONS FOR PRACTICE:

Applicable to this clinical practice:
- Since we as emergency physicians are the first to receive these patients from EMS, and will have patients who develop refractory ventricular fibrillation in the
emergency department, this article is applicable for us to take the correct approach at medically managing these patients.

- Clinically Relevant:
  - This was the first randomized controlled trial to compare amiodarone and lidocaine directly for the treatment of out-of-hospital cardiac arrest. Amiodarone is currently a drug of choice by AHA guidelines for refractory ventricular fibrillation. This article supported the use of amiodarone for this purpose and is still relevant today for that reason. The authors were able to show a survival advantage to admission but not to discharge. One proposed criticism was that this could lead to increased cost and suffering without long term benefit. It does however improve time to return of spontaneous circulation, which, with other adjunctive therapies could hypothetically help improve outcomes with additional advances in post-cardiac arrest care (i.e. therapeutic hypothermia). There is a high rate of poor neurologic outcomes in these groups and this study did not address neurologic outcomes for survivors.

**LEVEL OF EVIDENCE / DECISION FOR USE:**
- Background | Consider Replication | Ready for use

- Level of Evidence:
  - Ib Evidence obtained from at least one RCT