Determinants of Cardioversion Success for Atrial Arrhythmias

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Atrial Fibrillation

- Most commonly encountered arrhythmia in clinical practice.
- May occur in association with other arrhythmias such as atrial flutter or atrial tachycardia.
  - Aflutter may degenerate into AF
  - AF may convert to aflutter, particularly during treatment with anti-arrhythmic agents
  - AVRT and AVNRT may also trigger AF
Therapeutic Options

- Rate control (AFFIRM)
  - AV nodal blockers
  - AV nodal ablation and pacing

- Rhythm control
  - Pharmacologic cardioversion (usually class III or IC)
  - DC electrical cardioversion
  - RF catheter ablation
  - Surgical maze procedures

+ / - anticoagulation
Synchronized direct-current cardioversion is an effective method of converting atrial fibrillation to sinus rhythm.

Overall success rate (at any level of energy) for atrial fibrillation is 75–93%. 2

Success is inversely related to both the duration of atrial fibrillation and to left atrial size. 2
- Only 50% success if duration > 5 years 2
## Electrical Cardioversion Success

- Trial of 1,838 attempted cardioversions and success rates:

<table>
<thead>
<tr>
<th>Duration of atrial fibrillation</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 days</td>
<td>84%</td>
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<tr>
<td>30–90 days</td>
<td>78%</td>
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<tr>
<td>90–180 days</td>
<td>77%</td>
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<tr>
<td>&gt;180 days</td>
<td>66%</td>
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<tr>
<td>&gt;5 years</td>
<td>50%</td>
</tr>
</tbody>
</table>

Gallagher MM; Guo XH; Poloniecki JD; Guan Yap Y; Ward D; Camm AJ. Initial energy setting, outcome and efficiency in direct current cardioversion of atrial fibrillation and flutter. J Am Coll Cardiol 2001 Nov 1;38(5):1498–504.
Other factors possibly related to successful (electrical) cardioversion:

- Pre-treatment with AAD (anti-arrhythmic drugs)
  - Increase likelihood of successful cardioversion AND help to maintain sinus rhythm after cardioversion
  - Pre-treatment with amiodarone x1 month prior to cardioversion improved the reversion rate (88 versus 56 to 65 percent without pretreatment)$^{6}$
  - Ibutilide thought to lower defibrillation threshold; not used as much anymore due to 3% risk for Torsades$^{1}$
# Pre-treatment with AADs

**ACC/AHA/ESC guideline summary: Antiarrhythmic drug enhancement of direct-current (DC) cardioversion in atrial fibrillation (AF)**

<table>
<thead>
<tr>
<th>Class IIa - The weight of evidence or opinion is in favor of the usefulness of the following approaches to the pharmacologic enhancement of DC cardioversion in AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pretreatment with amiodarone, flecainide, ibutilide, propafenone, or sotalol, which may also prevent recurrent AF.</td>
</tr>
<tr>
<td>• In patients who relapse after successful cardioversion prior to repeat DC cardioversion.</td>
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<table>
<thead>
<tr>
<th>Class IIb - The weight of evidence or opinion is less well established for the usefulness of the following approaches for the pharmacologic enhancement of DC cardioversion in AF</th>
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<tbody>
<tr>
<td>• Among patients with persistent AF, beta blockers, disopyramide, diltiazem, doxetilide, procainamide, or verapamil; the ability of these drugs to increase the success of DC cardioversion or to prevent early AF recurrence is uncertain.</td>
</tr>
<tr>
<td>• Out-of-hospital initiation of antiarrhythmic drugs in patients without heart disease.</td>
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<tr>
<td>• Out-of-hospital initiation of antiarrhythmic drugs in patients with certain forms of heart disease if the safety of drug has been verified for the patient.</td>
</tr>
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Observational data suggested that ACEIs and ARBs may prevent both new onset AF and recurrent AF.

RCT of 1,442 patients with underlying CVD, DM, or left atrial enlargement in sinus rhythm with:
- ≥ 2 documented episodes of atrial fibrillation in the past 6 months OR
- successful cardioversion for atrial fibrillation in past 2 weeks

Recurrence of atrial fibrillation (followed 1 year):
- 51.4% valsartan group
- 52.1% placebo group

Treatment with valsartan NOT associated with a reduction in incidence of recurrent atrial fibrillation.

Electrical Cardioversion Success – Electrode Positions

1999 Prospective Randomized Trial UK\(^6\)
- 90 patients to anteroanterior v. anteroposterior
- Initial shock 100 J (then 200, 300, 360).
  - *Conclusion*: Electrode pad position is NOT a determinant of cardioversion success.

2002 Randomized Trial Germany\(^7\)
  - *Conclusion*: Anteroposterior more successful (96%) than anterolateral (78%).

**BOTTOM LINE: EQUIVOCAL**
Obese patients require higher energy for successful cardioversion.\textsuperscript{9}

- In one study of 110 patients, cardioversion with $\leq 200$ Joules was more successful in patients weighing less than 71 kg than in those weighing over 100 kg (78 versus 25 percent).
- The odds ratio for cardioversion failure was 1.5 for every 10 kg increment in body weight.

Suggestions:
- For patients weighing $\leq 85$ kg, initial energy should be 200 Joules.
- Those weighing 86 to 100 kg, initial energy should be 360 Joules.
- Those $> 100$ kg should receive adjunctive measures, such as pretreatment with an anti-arrhythmic drug, in conjunction with an initial shock of 360 Joules.
Role of Sleep Apnea in AF

- Approximately $\frac{1}{2}$ of patients with atrial fibrillation are likely to have OSA.
  - The association of OSA with AF was greater than the association of OSA with traditional risk factors such as BMI, neck circumference, and HTN.

- Obesity and the magnitude of nocturnal oxygen desaturation are independent risk factors for AF.

- OSA an independent risk factor for recurrence of atrial fibrillation after cardioversion.
  - Those treated with CPAP had reduction in recurrence of atrial fibrillation 1 year s/p cardioversion


Purpose

- To investigate predictors of transthoracic cardioversion success in atrial fibrillation, atrial flutter, and atrial tachyarrhythmias between *January 1, 1998 and December 31, 2008* at the University of Washington Medical Center.
Methods

- Retrospective analysis of medical records at the University of Washington of patients who underwent elective DC cardioversion for atrial arrhythmias between 6/2004 to 12/2008
  - Records identified by billing department codes
  - Clinical data extracted by myself
  - Stored in a secure database (George Johnson)

- What are predictors of (first–shock) cardioversion success for atrial arrhythmias?
  - Hypothesis–generating (not testing a specific hypothesis)
Clinical data collected:
- Demographics
- Baseline labs
- Baseline clinical variables (medical hx, cardiac surgical hx, cardioversion hx, ablation hx, atrial arrhythmia hx, medications, smoking hx, etc.)
- Echocardiographic data (LVEF, LA diameter, valvular disease, systolic or diastolic dysfunction, pulmonary HTN, right heart failure)
- Cardioversion procedure data
  - Anesthetic used
  - Physician performing the cardioversion (ER, EP, Cardiology)
  - Number of attempts, energy used
  - Electrode positions
  - Shock success (defined as absence of reversion to atrial arrhythmia in next 15 minutes)
Continuous variables were log-transformed if their distribution departed from normality. The means between those with success during electrical cardioversion and those who failed were tested for equality using a t-test with unequal variance adjustments; highly skewed continuous variables were analyzed using the non-parametric Wilcoxon rank sum test, which tests to see if the cases and controls came from populations with the same distribution.

The Fisher's exact test was used to test for an association between success during electrical cardioversion and binary variables of interest. We estimated the odds ratio of being success comparing the "yes" category with the baseline "no" category of each given binary variable of interest. The 95% confidence intervals (CI) are provided along with 2-sided and 1-sided p-values.

We tested the association of being a success with unordered categorical variables using Pearson's chi-squared test. Also, we tested the association of being a success with ordered categorical variables by using a test of homogeneity of odds of being a case among all categories of the given variable. A test of trend was also performed.
Results

131 charts reviewed

- 10 (inpatient, monitored internal cardioversion)

121 included

74.4% first-shock success rate

90 first-shock success

31 no first-shock success
Results

- 74.4% successful cardioversion (first-shock)
  - Increased to 90% with two shocks.
    - Increased to 92.6% with three shocks.

- Maximum shocks = 4.

- Increasing energy with each shock (means):
  - 198 J first shock
  - 259 J second shock
  - 298 J third shock
<table>
<thead>
<tr>
<th></th>
<th>All Patients n=121</th>
<th>First-Shock Success n=90</th>
<th>No First-Shock Success n=31</th>
<th>OR and CI, and p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (% male)</td>
<td>77.7%</td>
<td>78.8%</td>
<td>74.2%</td>
<td></td>
</tr>
<tr>
<td>Age (avg +/- SD)</td>
<td>58 +/- 13</td>
<td>58 +/- 13</td>
<td>58 +/- 14</td>
<td></td>
</tr>
<tr>
<td>BMI (avg +/- SD)</td>
<td>28.3 +/- 6.1</td>
<td>28.3 +/- 5.3</td>
<td>28.6 +/- 8.0</td>
<td></td>
</tr>
<tr>
<td>History of AF</td>
<td>81.8%</td>
<td>82.2%</td>
<td>80.6%</td>
<td></td>
</tr>
<tr>
<td>History of AFlutter</td>
<td>25.6%</td>
<td>30.0%</td>
<td>12.9%</td>
<td>2.89 (0.88 to 12.38) p = 0.05</td>
</tr>
<tr>
<td>History of Other AT</td>
<td>8.3%</td>
<td>7.8%</td>
<td>14.3%</td>
<td></td>
</tr>
<tr>
<td>LVEF (%) (avg +/- SD)</td>
<td>54.7 +/- 13.7 n=114</td>
<td>55.0 +/- 13.4 n=83</td>
<td>53.9 +/- 14.6 n=31</td>
<td></td>
</tr>
<tr>
<td>LA size (cm) (avg +/- SD)</td>
<td>4.72 +/- 0.87 n=97</td>
<td>4.70 +/- 0.89 n=71</td>
<td>4.79 +/- 0.83 n=26</td>
<td></td>
</tr>
<tr>
<td>Pre-shock rhythm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AF</td>
<td>77.7%</td>
<td>75.6%</td>
<td>83.9%</td>
<td></td>
</tr>
<tr>
<td>Aflutter</td>
<td>21.5%</td>
<td>23.3%</td>
<td>16.1%</td>
<td></td>
</tr>
<tr>
<td>Other AT</td>
<td>0.8%</td>
<td>1.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (Joules) (avg +/- SD)</td>
<td>198 +/- 74</td>
<td>198 +/- 77</td>
<td>198 +/- 68</td>
<td></td>
</tr>
</tbody>
</table>
# Results – Pre-shock Rhythm

<table>
<thead>
<tr>
<th></th>
<th>Atrial Fibrillation (n=94)</th>
<th>Atrial Flutter (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} shock efficacy</td>
<td>72.3%</td>
<td>84.6%</td>
</tr>
<tr>
<td>2\textsuperscript{nd} shock efficacy</td>
<td>90.4%</td>
<td>92.3%</td>
</tr>
</tbody>
</table>
Results – Duration of Arrhythmia

\[ p = 0.04 \]

<table>
<thead>
<tr>
<th>Percent (%)</th>
<th>≤ 2 days</th>
<th>&gt;2 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>30%</td>
<td>60%</td>
</tr>
<tr>
<td>1st shock success</td>
<td>30%</td>
<td>60%</td>
</tr>
<tr>
<td>Unsuccessful</td>
<td>30%</td>
<td>60%</td>
</tr>
</tbody>
</table>
Weak but potential trends associated with first-shock success (NOTE: these are not (yet) statistically significant):

- More hypercholesterolemia (1.76, 95% CI (0.71–4.34)).
  - Probably due to more statin use (1.76, 95% CI (0.69–4.66)).
- Less mitral valve disease (0.62, 95% CI (0.22–1.62)).
- Less pulmonary HTN (0.59, 95% CI (0.23–1.59)).
Results – Statistics

- History of atrial flutter, OR 2.89.
  - Sample size 194 to claim significance.

- Duration of arrhythmia, significant by Pearson’s chi-squared test for unordered categorical variables.

- To justify the relationship between history of hyperlipidemia and cardioversion success, OR 1.76.
  - Sample size 436 needed.
Discussion

- History of atrial flutter and association with success?

- Is statin use associated with greater success in DC cardioversion of atrial arrhythmias?

- Is the presence of more pulmonary HTN (even mild) in the unsuccessful cardioversion group due to more mitral valve disease (regurgitation) or to potentially undiagnosed OSA?

- Many more…
Next Steps

- Review more cardioversions to better power the results (n=121 now). Have not met 1998–2008 goal (n>500).

- Then perform a step-wise regression, multi-variable analysis of all co-variables to generate hypotheses.

- Generate ≥ one hypothesis that can be further investigated with a RCT or case-control study.
Acknowledgements

- Dr. Jeanne Poole

- Jia Yin (Angel) Wan
  - Center for Biomedical Statistics
  - Institution for Translational Health Sciences

- George Johnson, B.S.E.E.
  - Seattle Institute of Cardiac Research

- Department of Internal Medicine


6. Mathew TP; Moore A; McIntyre M; Harbinson MT; Campbell NP; Adgey AA; Dalzell GW. Randomised comparison of electrode positions for cardioversion of atrial fibrillation. Heart 1999 Jun;81(6):576–9.


92 patients with atrial fibrillation > 2 weeks duration assigned to 1 of 3 groups:

- A: oral amiodarone 400 mg daily x1 month before and 200 mg x2 months after
- B: oral diltiazem 180 mg daily x1 month before and x2 months after, 80 mmol potassium, 50 UI insulin in 500 ml 30% glucose solution 24h prior
- C: oral diltiazem 180 mg daily x1 month before and x2 months after

Findings:

- Electrical cardioversion was more successful in group A (88%) than groups B (56%) or C (65%) (p<0.05).
- Electrical thresholds were lower in group B.
- 24 hours after cardioversion, the early recurrence of atrial fibrillation was similar in the three groups.
- Before electrical cardioversion, the rate of spontaneous conversion to sinus rhythm was higher in group A (25%) than in groups B (6%) or C (3%).
Ibutilide Pre-treatment

- **Ibutilide**: A Class III anti-arrhythmic
- 100 patients with atrial fibrillation for a mean of 117+/-201 days randomly assigned to undergo transthoracic cardioversion with or without pre-treatment with 1 mg ibutilide (Oral, et al.)
  - Success 72% without ibutilide.
  - Success 100% with ibutilide.
- Sustained polymorphic ventricular tachycardia in 3% patients who received ibutilide.
  - LV ejection fraction \( \leq 20\% \).
  - ↑QTc interval in treated group (482±49 v. 432±37 msec)
- Other Studies: 3.6–8.3% risk of Torsades
- Limitations: Many patients concurrently being treated with other anti-arrhythmics (synergistic effect?).
Biphasic waveforms defibrillate more effectively and at lower energies than monophasic waveforms in cardioversion of AF.

- Prior to 2000, only monophasic defibrillators.
- Biphasic not yet standard as most centers have not yet replaced the monophasic machines with biphasic.
- University of Washington hospital switch-out:
  - 10/2003 EP lab
  - 1/2005 hospital-wide
  - 1st shock efficacy greater with biphasic (no difference in cumulative shock efficacy).
  - At $\leq 200$ J, biphasic more effective. No difference in efficacy between 200J biphasic and 360 J monophasic.
  - No additional efficacy with biphasic for cardioversion of atrial flutter (but decreased skin burns).
  - Biphasic results in less cardiac stunning.
  - Monophasic still highly effective in most situations.
  - Unclear that the superior efficacy of biphasic results in important clinical advantages.
Diastolic dysfunction
- “impaired relaxation”
- ≥ mild diastolic dysfunction

Systolic dysfunction
- ≥ mild systolic dysfunction
- “systolic heart failure”
- ischemic and non–ischemic cardiomyopathies

CAD
- History of MI, +stress test, +cardiac cath (more than diffuse mild luminal irregularities), wall–motion abnormalities on TTE from suspected ischemia (absence of non–ischemic cardiomyopathy)
There is suggestive evidence of an association between having success and duration of current episode (p=0.08, chi-squared homogeneity of odds).

There is evidence of a decrease in the odds of having a success as the duration of the current episode increased (p=0.04, test of trends).
Results – Location of CV

- Unclear if location matters (ED v. PACU).
  - My observations (through chart review) of cardioversions in the ED:
    - usually lone atrial fibrillation in an otherwise (and generally young) healthy individual
    - patient very certain of onset of arrhythmia being less than 48 hours ago
    - etomidate or fentanyl/versed combination versus propofol in the PACU
    - lower energy levels
  - Needs further analysis, higher power.
Results – Past Medical Hx

- Gross observations associated with first-shock success:
  - Less diabetes (though not less CAD).
  - More hyperlipidemia (?more statin use).
  - Less current/past smokers.
  - Less non-ischemic cardiomyopathy.
  - Less systolic dysfunction.
  - Less valvular disease.
  - More CAD (?medications).
  - Less pulmonary HTN.
  - More CPAP use (n=11 only).
  - Fewer ablations for atrial arrhythmias.
Discussion

- History of atrial flutter and association with success?
  - Could this be atrial flutter with variable block (sometimes difficult to distinguish from AF on EKG)?
  - Or do patients with a history of atrial flutter have more organization to their AF compared to those with just AF?

- Is statin use associated with greater success in DC cardioversion of atrial arrhythmias?
  - A 2007 meta-analysis (JACC) suggests that increased CRP levels are associated with greater risk of AF recurrence.

- Is the presence of more pulmonary HTN (even mild) in the unsuccessful cardioversion group due to more mitral valve disease (regurgitation) or to potentially undiagnosed OSA?

- Many more...