Atrial Fibrillation: An Evidence Based Approach to Comprehensive Management

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Just a Thought

Link your roots deeply into whatever task you are doing, for commitment and enthusiasm transform monotony into freshness and routine into joy and discovery.
Atrial Fibrillation

♥ Rapid, irregular fib waves
♥ Atrial rate > 350
♥ Fib wave seen best in V1
♥ Irregularly irregular ventricular rate
♥ QRS usually normal
♥ If QRS is wide and rate > 200 then consider WPW with conduction over accessory pathway

ECG Recognition of AF
Atrial fibrillation can be Coarse or Fine

Fast or Slow
Conduct Aberrantly

Not conduct at all
Occurs intermittently

The Scope

♥ The most frequently occurring arrhythmia
♥ 2.2 million adults in the US have AF
• 0.4% - 1% of the general population
• 70% of cases occur in people 65-85 years old
  • < 0.1% in people < 55 years old
  • 9% - 10% in people > 80 years old
• More common in men than women
• More common in Caucasians

Many people have it, it's a chronic problem, and what do you do about it?
Classification

♥ Paroxysmal
  • Terminates spontaneously or with intervention

♥ Persistent
  • When sustained beyond 7 days

♥ Long Standing Persistent
  • When it lasts longer than one year

♥ Permanent
  • Joint decision by clinician and patient to accept atrial fibrillation / no further attempts at cardioversion

♥ Recurrent
  • Two or more episodes of paroxysmal or persistent AF

♥ “Lone AF”
  • Young adults without clinical or echocardiographic evidence of cardiopulmonary disease

Mechanisms of AF
Requires a “trigger” and an anatomic substrate capable of initiating and maintaining AF

♥ Enhanced automaticity
  • Rapid firing of foci in or near the pulmonary veins in LA (most common site)
  • Other common sites: in posterior wall of LA, RA, SVC, coronary sinus

♥ Reentrant circuits
  • One or more reentry circuits within the atria with “wavelets” that spread in multiple directions
**Paroxysmal AF**

- Pathological triggers repeatedly initiate AF
- Triggers often related to autonomic nervous system
- Patients often younger and without structural heart disease
- About 25% of patients with paroxysmal AF progress to permanent AF within 5 years

**Persistent & Permanent AF**

- Involve abnormal atrial substrate that perpetuates AF
- Atrial enlargement with fibrosis
- **Multiple reentry circuits**
- Abnormal triggers located in extra-atrial sites (i.e. pulmonary veins)

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**Trigger Sites**

**Posterior view of atria**

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- Left superior pulmonary vein
- Left inferior pulmonary vein
- Right superior pulmonary vein
- Right inferior pulmonary vein
- Coronary Sinus
- SVC
- IVC
Reentry Circuits

- Left superior pulmonary vein
- Left inferior pulmonary vein
- Right superior pulmonary vein
- Right inferior pulmonary vein
- Coronary Sinus
- SVC
- IVC

Pathophysiology

- **Inflammation**
  - C-reactive protein levels higher in persistent AF patients
- **Autonomic nervous system**
  - Stimulation of parasympathetic system shortens atrial and PV refractory periods
- **Atrial ischemia**
- **Atrial dilation from volume overload**
- **Structural changes associated with aging**
Pathophysiology

♥ Atrial fibrosis and loss of atrial muscle mass.
♥ Triggers of fibrosis include
  - Inflammation / Autoimmune disorders
  - Atrial dilation
  - Atrial ischemia
  - Aging
♥ AF itself causes alterations in atrial architecture and function contributing to atrial remodeling
♥ “Atrial fib begets atrial fib”
  • Atrial electrical remodeling
  • Progressive shortening of effective refractory periods

Causes

♥ Reversible
  • Alcohol intake
  • Surgery (common in cardiac surgery)
  • Electrocution
  • Acute MI
  • Pericarditis
  • Myocarditis
  • Pulmonary Embolism
  • Other pulmonary diseases
  • **Obstructive sleep apnea**
  • Hyperthyroidism
  • A flutter
  • WPW
  • AVNRT

♥ Obesity
  • LA size increases as BMI increases

♥ Without associated Heart Disease
  • “Lone AF”
  • Familial arrhythmia
Associated Heart Disease

- Valvular heart disease • Most often mitral valve
- HF
- CAD
- HTN • Especially if LVH present
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Restrictive cardiomyopathy
- Constrictive pericarditis
- Cardiac tumors
- Congenital diseases • Atrial septal defects

Hemodynamic Consequences

- Loss of synchronous atrial mechanical activity • Loss of atrial contraction • Compounded in cases of mitral stenosis, aortic stenosis, HTN, HCM, restrictive cardiomyopathy
- Irregular ventricular response • Cardiac output falls
- Rapid heart rate
- Impaired coronary arterial blood flow • Diastolic duration inconsistent and unreliable • Increased coronary vascular resistance
Stroke: The Most Devastating Complication of AF

♥ Atrial fibrillation is an independent risk factor for stroke: increases risk about five-fold.
♥ AF is responsible for >15% of all strokes
♥ Strokes associated with AF are more severe and TIAs last longer than those due to carotid disease
♥ Strokes associated with AF have more disability and higher mortality than strokes that occur in absence of AF
### Atrial Fibrillation

<table>
<thead>
<tr>
<th>Rate Control</th>
<th>Rhythm Control</th>
<th>Prevention of Thromboembolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Calcium Channel Blockers (2)</td>
<td>● Electrical or chemical cardioversion</td>
<td>● All patients regardless of rate or rhythm control</td>
</tr>
<tr>
<td>● Beta Blockers</td>
<td>- Chemical effective if atrial fib &lt; 7 days</td>
<td>● Amount of time in atrial fibrillation is not deciding factor</td>
</tr>
<tr>
<td>● Always first priority</td>
<td>- TEE guided or full anticoagulation</td>
<td>● Decision based on stroke risk</td>
</tr>
<tr>
<td>● Strict versus lenient rate control</td>
<td>● Class I and Class III antiarrhythmics</td>
<td>● CHADS2</td>
</tr>
<tr>
<td>- RACE II</td>
<td>● AFFIRM and RACE trials</td>
<td>● CHADS Vasc Score</td>
</tr>
<tr>
<td>- 2014 New Guideline Recommendation</td>
<td>● Registry data supports slowing progression of disease</td>
<td></td>
</tr>
<tr>
<td>● AV node ablation if pharmacological therapy cannot control rate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Evidence and Application


- *Get with Guidelines Atrial Fibrillation Quality Improvement Program*
Rate Control

♥ Avoid development of tachycardia-induced cardiomyopathy
♥ Avoid toxic effects of antiarrhythmics
♥ Accomplished through medications that slow conduction through the AV node
  • Beta blockers, calcium channel blockers (verapamil, diltiazem) most common
  • Digoxin only effective at rest
♥ Pacemaker may be required if HR becomes too low
♥ AV Ablation is an option if pharmacological therapy is unsuccessful in controlling rate
♥ Continued anticoagulation required

A Closer Look at Calcium Channel Blockers

<table>
<thead>
<tr>
<th></th>
<th>Verapamil</th>
<th>Dihydropyridines</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>▼▼</td>
<td>▲</td>
<td>▼</td>
</tr>
<tr>
<td>AV Nodal Conduction</td>
<td>▼▼</td>
<td>------</td>
<td>▼</td>
</tr>
<tr>
<td>Contractility</td>
<td>▼▼</td>
<td>▼</td>
<td>▼</td>
</tr>
<tr>
<td>Arterial Vasodilatation</td>
<td>▲▲</td>
<td>▲▲▲</td>
<td>▲</td>
</tr>
</tbody>
</table>
Pharmacological Considerations in Rate Control

♥ Calcium channel blockers versus beta blockers

♥ Pros and Cons of Digoxin
  • Blood pressure effect
  • Heart rate control at rest versus exercise

♥ Pros and Cons of Amiodarone
  • Limiting use of other antiarrhythmics (terminal half-life elimination 40 to 55 days)
  • Use in heart failure

Additional Rate Control Information

RACE II
♥ Strict versus lenient rate control

♥ Strict
  • Resting HR < 80
  • Exercise < 110

♥ Lenient
  • Resting HR < 110

♥ No benefit of strict rate control

♥ Note: Study population did not include high % of patients with heart failure.
Class III Recommendation:

Treatment to achieve strict rate control of heart rate (<80 bpm at rest or <110 bpm during a 6-minute walk) is not beneficial compared to achieving a resting heart rate <110 bpm in patients with persistent AF who have stable ventricular function (left ventricular ejection fraction >0.40) and no or acceptable symptoms related to the arrhythmia, though uncontrolled tachycardia may over time be associated with a reversible decline in ventricular performance (Level of Evidence: B)

New 2014 Guideline Update

A randomized trial suggested that a lenient (<110 bpm) rate control strategy was as effective as a strict strategy (<80 bpm) in patients with persistent/permanent AF. However, the writing committee still advocates for the latter (Class IIa), as the results of this single trial were not thought to be definitive.
Rhythm Control

♥ Prevention of thrombus formation
♥ Prevention of atrial myopathy
♥ Relief of symptoms
♥ Initially mechanical cardioversion without antiarrhythmics
♥ Subsequent occurrences attempt cardioversion with antiarrhythmics
♥ Antiarrhythmics – toxic side effects

AFFIRM Trial (2002)

♥ Compared rate control and rhythm control in patients with AF to determine which approach was associated with better survival outcome

♥ Results

• Mortality rate nearly equal in the two groups
• More ischemic strokes in rhythm control group (anticoagulation often DC’d with NSR)
• More adverse drug effects in rhythm control group
• More hospitalizations in rhythm control group
**AFFIRM**

**Conclusions:**

- Rhythm control offers no survival advantage over rate control
  - Trend toward increased mortality with rhythm control
- Potential advantages to rate control: fewer adverse drug effects
- Anticoagulation should be continued in all AF patients at risk for stroke regardless of rate or rhythm control strategies

**RACE (2002)**

**Compared rate control and rhythm control in patients with recurrent persistent AF**

- End point was composite of CV death, admission for HF, thromboembolic event, severe bleeding, severe side effects from drugs

**Results:**

- Primary end point occurred in 17.2% of rate control group and 22.6% of rhythm control group (trend in favor of rate control)
- Thromboembolism more frequent in rhythm control group
- More adverse drug effects in rhythm control group
Conclusions:

- Rate control is not inferior to rhythm control for prevention of death and morbidity from CV causes in patients with persistent AF
- Cardiovascular risk (including risk of stroke) is not reduced with rhythm control even when sinus rhythm is maintained
- Anticoagulation therapy should continue in all AF patients at risk for stroke regardless of rate or rhythm control therapy

Rate Vs Rhythm Control Recommendations

- Data from 7 trials do not support a routine strategy of rhythm control in patients with atrial fibrillation with or without HF
- Rate control recommended in most patients with AF
- Rhythm control can be considered based on specific patient considerations
  - Continuing symptoms on rate control
  - Exercise intolerance with rate control drugs
  - Patient preference
Registry data showing support for rhythm control in select patients to decrease disease progression. *(Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation)*

**HOWEVER!**

**Anticoagulation Decision Making**

- ♥ Chronic anticoagulation is recommended in both groups in patients at high risk for stroke
- ♥ C – HF / LVEF ≤ 35%
- ♥ H – Hypertension
- ♥ A – Age
- ♥ D – Diabetes Mellitus
- ♥ S₂ - Stroke or TIA
In assessing risk of stroke in a patient with nonvalvular AF, the writing committee recommends (Class I) the usage of the CHA$_2$DS$_2$-VASc (C=congestive heart failure; H=hypertension; A$_2$=age $\geq$75 years [doubled]; D=diabetes mellitus; S$_2$=stroke, transient ischemic attack, or thromboembolism [doubled]; V=vascular disease; A=age 65-74 years; Sc=sex category, i.e., female gender) score, as opposed to the CHADS$_2$ score.
Point 2

For nonvalvular AF patients with a history of stroke or transient ischemic attack, or a CHA$_2$DS$_2$-VASc score $\geq 2$, oral anticoagulation is recommended (Class I). Options for oral anticoagulation include warfarin, dabigatran, rivaroxaban, and apixaban.

Point 3

For patients with nonvalvular AF and a CHA$_2$DS$_2$-VASc score of 0, it is reasonable to omit antithrombotic therapy (Class IIa).
Point 4

The following options may be considered with a patient with nonvalvular AF and a CHA$_2$DS$_2$-VASc score of 1: no antithrombotic therapy, oral anticoagulation, or aspirin (Class IIb).

Point 5

None of the new novel oral anticoagulants (dabigatran, rivaroxaban, or apixaban) are recommended to be used in patients with AF and a mechanical or bioprosthetic heart valve (Class III harm).
Point 6

Oral anticoagulation should be prescribed to patients with hypertrophic cardiomyopathy and AF irrespective of the CHA$_2$DS$_2$-VASc score (Class I).

General Principles for Atrial Arrhythmias

♥ Critical care setting associated with increased catecholamine levels
- Treat infection
- Treat inflammation
- Correct electrolytes
### Antiarrhythmics in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Class</th>
<th>Specific Medications</th>
<th>Purpose of Medication</th>
<th>Major Cardiac Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IA</td>
<td>Disopyramide</td>
<td>Rhythm Control</td>
<td>Torsade de pointes, HF</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Quinidine</td>
<td></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Class IB</td>
<td>Flecainide</td>
<td></td>
<td>Ventricular tachycardia, HF, Atrial Flutter</td>
</tr>
<tr>
<td></td>
<td>Propafenone</td>
<td></td>
<td>Ventricular tachycardia, HF, Atrial Flutter</td>
</tr>
<tr>
<td>Class IC</td>
<td></td>
<td>Rhythm Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>Beta Blockers</td>
<td>Rate Control</td>
<td>Torsade de pointes (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>* Organ toxicity</td>
</tr>
<tr>
<td>Class III</td>
<td>Amiodarone</td>
<td>Rhythm / Rate Control</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Dronedarone</td>
<td></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Dofetilide</td>
<td></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Ibutilide</td>
<td></td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td></td>
<td>Sotalol (Also contains beta blocker)</td>
<td>Rhythm Control (also controls rate)</td>
<td>Torsade de pointes, HF, Beta blocker side effects</td>
</tr>
<tr>
<td>Class IV</td>
<td>Calcium Channel Blockers</td>
<td>Rate Control</td>
<td></td>
</tr>
</tbody>
</table>

Medications Used to Maintain Sinus Rhythm in Patients with Atrial Fibrillation

- Amiodarone
- Disopyramide
- Dofetilide
- Dronedarone
- Flecainide
- Procainamide
- Propafenone
- Quinidine
- Sotalol
New Guideline Clarification

As in the earlier guidelines, the committee recommends against the use of certain antiarrhythmic medications (flecainide, propafenone, dofetilide, and sotalol) in patients with severe left ventricular hypertrophy (LVH). In the current guidelines, severe LVH is now defined as wall thickness exceeding 1.5 cm.
Class I: Na⁺ Channel Blockers

Class III: K⁺ Channel Blockers

Class IV: Calcium Channel Blockers

Marked prolongation of refractory period (prolong QT interval).

Slow conduction (widen QRS).
Some prolongation of refractory period (prolong QT interval).
Antiarrhythmic Medications Effecting the Action Potential

- **Class I** – Fast sodium channel blockers
  - IA: Quinidine, Procainamide, Disopyramide
  - IB: Lidocaine, Mexiletine, Tocainide
  - IC: Flecainide, Propafenone

- **Class III** – Potassium channel blockers
  - Amiodarone, Dronedarone, Ibutilide, Dofetalide, Sotalol

- **Class IV** – Calcium channel blockers
  - Verapamil, Diltiazem

Effects of Class I Antiarrhythmics

- **All Class 1 antiarrhythmics by definition block the fast sodium channel**
  - Different drugs do this to a different degree
  - IC > IA > IB

- **Blocking of the fast sodium channel interferes with rapid depolarization and decreases conduction velocity**
  - This will increases the duration of the cardiac action potential
  - Note: This effect is seen in the action potential of the purkinge fibers but not in the action potential of the nodal tissue
Benefits of Reducing Rate and Degree of Depolarization

♥ Decrease in conduction velocity in non-nodal tissue is called negative dromotropy.

♥ This is suppress reentrant tachycardias because reentrant tachycardias are caused by abnormal conduction.

Effects of Class 1 Antiarrhythmics

♥ In addition to blocking the fast sodium channel (Phase 0) – some class I agents also block the potassium channel (Phase 3)

♥ Potassium channel blockade directly affects the duration of the cardiac action potential and the effective refractory period.

♥ Benefits and disadvantages of effecting refractory period
  • Beneficial in reentrant tachycardias
  • Can increase risk for Torsades

♥ Different drugs do this to a different degree
  • IA (increase refractory period) > IC (no effect) > IB (decrease refractory period)
Effects of Class 1 Antiarrhythmics

Depression of Automaticity

♥ Can suppress abnormal automaticity
♥ Not related to sodium channel effect
♥ Mechanism not fully understood

Anticholinergic Effect

♥ Strong inhibitors of vagal activity
♥ Offsets some of benefit (i.e. an increase ventricular rate during the treatment of atrial arrhythmias)
♥ Can increase SA rate and conduction through the AV node

Class I C Antiarrhythmics

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Potent inhibition of fast sodium channel; decrease in maximal rate of phase 0 depolarization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Slow His-Purkinge conduction and cause QRS widening; QT intervals are also usually prolonged</td>
</tr>
<tr>
<td></td>
<td>No effect on refractory period</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic effects</td>
</tr>
<tr>
<td>Uses</td>
<td>Life threatening ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Conversion to SR (Flecainide)</td>
</tr>
<tr>
<td>Drugs</td>
<td>Flecainide (Tambocor)</td>
</tr>
<tr>
<td></td>
<td>Moricizine (Ethomozine)</td>
</tr>
<tr>
<td></td>
<td>Propafenone (Rhythmol)</td>
</tr>
</tbody>
</table>
Class I C Antiarrhythmics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flecaainide (Tambocor)</td>
<td>Not a first line agent for ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Will slow conduction over accessory pathways in WPW tachycardias</td>
</tr>
<tr>
<td></td>
<td>Used in atrial fibrillation (pill in the pocket)</td>
</tr>
<tr>
<td></td>
<td>CAST Trial: propensity for fatal proarrhythmic effects</td>
</tr>
<tr>
<td></td>
<td>Not used post MI or with depressed LV function</td>
</tr>
<tr>
<td>Moricizine (Ethmozine)</td>
<td>CAST studies: Reserved for life threatening ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Has properties of class I B also</td>
</tr>
<tr>
<td>Propafenone (Rhythmol)</td>
<td>Used in supraventricular arrhythmias and life threatening ventricular arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Also has small beta blocking actions and calcium channel blocking effects that can worsen HF</td>
</tr>
<tr>
<td></td>
<td>Must be initiated in hospital setting to monitor ECG if any structural heart disease</td>
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</tbody>
</table>

Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Action Potential</th>
<th>Inhibits potassium ion fluxes during phase II and III of the action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Directly on myocardium to delay repolarization (prolongs QT); prolongs effective refractory period in all cardiac tissue; By definition act only on repolarization phase and should not impact conduction</td>
</tr>
<tr>
<td>Cautions</td>
<td>Proarrhythmic Effects (amiodarone less)</td>
</tr>
<tr>
<td>Uses</td>
<td>Drug dependent</td>
</tr>
<tr>
<td>Drugs</td>
<td>Amiodarone (Pacerone, Cordorone)</td>
</tr>
<tr>
<td></td>
<td>Dronedarone (Multaq)</td>
</tr>
<tr>
<td></td>
<td>Ibutilide (Corvert) – pure class III</td>
</tr>
<tr>
<td></td>
<td>Dofetilide (Tikosyn) – pure class III</td>
</tr>
<tr>
<td></td>
<td>Sotalol (Betapace)</td>
</tr>
</tbody>
</table>
## Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Amiodarone (ARREST Trial)</th>
<th>Approved for life threatening refractory ventricular arrhythmias; considered before lidocaine in pulseless VT or V fib; considered ahead of lidocaine for stable VT with impaired cardiac function; expanded to atrial and ventricular arrhythmias, conversion and maintenance of atrial fibrillation.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Use in atrial fibrillation is off label</strong></td>
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<tr>
<td></td>
<td>Slows conduction in accessory pathways</td>
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<td></td>
<td>Originally marketed as anti-anginal (potent vasodilator)</td>
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<tr>
<td></td>
<td>Relaxes smooth and cardiac muscle, reduces afterload and preload (well tolerated in heart failure and cardiomyopathy)</td>
</tr>
<tr>
<td></td>
<td><strong>Proarrhythmias less frequent</strong></td>
</tr>
<tr>
<td></td>
<td>Is also a weak sodium channel blocker, also has effects similar to class II and IV, also has anticholinergic properties</td>
</tr>
</tbody>
</table>

### More on Amiodarone

- Peripheral IV concentration not to exceed 2mg/ml

- Oral administration = GI symptoms
Potential Extra Cardiac Effects

<table>
<thead>
<tr>
<th>Pulmonary toxicity without initial symptoms / Potentially lethal interstitial pneumonitis /</th>
<th>Photosensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity</td>
<td>Corneal micro deposits</td>
</tr>
<tr>
<td></td>
<td>Optic neuropathy / neuritis</td>
</tr>
<tr>
<td></td>
<td>Thyroid dysfunction</td>
</tr>
</tbody>
</table>

Toxic side effects increase with length of use and increased dose

HOT OFF THE PRESS

New 2014 Atrial Fibrillation Guidelines

CHANGE IN
RECOMMENDATION
REGARDING AMIODARONE
FOR PATIENTS WITH PRE-EXCITATION
Lethal Outcome After Intravenous Administration of Amiodarone in Patient with Atrial Fibrillation and Ventricular Preexcitation

MUJOVIĆ NEBOJŠA M.D.¹,
SIMIĆ DRAGAN M.D.¹,
ANTONJEVIĆ NEBOJŠA M.D.¹ and
ALEMPJEVIĆ TAMARA M.D.²

Journal of Cardiovascular Electrophysiology

Volume 22, Issue 9, pages 1077–1078, September 2011

Article first published online: 18 FEB 2011
DOI: 10.1111/j.1540-8167.2011.02013.x
Postoperative CABG AF

♥ 20% to 50% of patients
♥ Almost always within 5 days
♥ Peak time: 2 days
♥ Increased risk morbidity
  • Up to 4 × risk for disabling embolic stroke
♥ Increased risk mortality
  • Up to 3 × risk for cardiac related mortality
♥ Most patients (without pre-existing AF) convert within 6 weeks

Postoperative CABG AF

♥ Class I Recommendations
  • Unless contraindicated, treatment with an oral beta blocker at least 24 hours before CABG to prevent post-operative AF is recommended for patients undergoing cardiac surgery.
    — Continued post operatively and at hospital discharge
  • Administration of AV nodal blocking agents is recommended to achieve rate control in patients who develop post-operative AF.

♥ Class IIa Recommendations
  • Preoperative administration of amiodarone is appropriate prophylactic therapy for patients at high risk for postoperative AF.
  • Digoxin and calcium channel blockers can be used for rate control
Inpatient Dosing Regimes in Atrial Fibrillation

Cardioversion

♥ PO - 1.2 to 1.8 g/day in divided doses until 10g total – then 200mg to 400mg daily for maintenance
♥ Or: PO 400mg TID x 5 to 7 days, then 400mg daily x 1 month, then 200mg daily

Post Op Prevention

♥ Post op: PO 400mg BID for up to 7 days
♥ Or: Start 7 days preoperatively 600mg PO per day and convert to 200mg per day until hospital discharge
♥ Or: IV – 1000mg/24 hours x 2 days

Note: Amiodarone use in atrial fibrillation is off label.

Class III Antiarrhythmics

<table>
<thead>
<tr>
<th>Ibutilide (Corvert)</th>
<th>Indicated for rapid conversion of atrial fib or flutter to sinus rhythm; IV use only; also facilitated cardioversion (Don’t convert atrial fib or flutter of duration without anticoagulation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dofetilide (Tykosin)</td>
<td>More “pure” class III agent Conversion to and maintenance of SR in A fib and flutter Reserved for very symptomatic patients, monitored 3 days in hospital Widens the QT; cannot be given with many other drugs (prolong QT or inhibit metabolism or elimination); no negative inotropic effects, neutral effect on mortality from arrhythmias post MI and in in HF, can be used in this population to prevent worsening HF from atrial fibrillation</td>
</tr>
</tbody>
</table>
**CLINICAL PEARL**

ALWAYS check potassium level prior to use of ibutilide—potassium level should be in high normal range.

Simultaneous 2-lead ECG (leads II and V1) showing initiation and termination of torsade de pointes in patient in AF after ibutilide infusion.

Class III Antiarrhythmics

| Sotalol | Used in atrial arrhythmias and life threatening ventricular arrhythmias  
|         | Indicated for stable monomorphic VT or Polymorphic VT with normal QT in ACLS protocol  
|         | Non selective beta blocking agent with class III properties  
|         | Significant class III effects are only seen at doses ≥ 160 mg  
|         | Proarrhythmic potential (prolonged QT)  
|         | More effective in preventing reoccurring arrhythmias than several other drugs |

Dronedarone

♥ Similar to amiodarone without iodine component and less fat soluble
♥ Class III antiarrhythmic (K⁺ channel blocker) with effects from all four classes
♥ Less effective than amiodarone at maintaining sinus rhythm but also less toxic
♥ Elimination half-life 13-19 hours
♥ Has both rate and rhythm control effects but is primarily indicated for rhythm control
♥ May reduce incidence of stroke (mechanism uncertain)
Dronedarone (ATHENA)

- Approved for maintenance of sinus rhythm in patients with history of paroxysmal or persistent AF or flutter with EF > 35% who are in sinus rhythm or will be cardioverted
- Dose: 400 mg PO bid with meals
  - Avoid grapefruit juice
  - Multiple drug interactions
- Contraindicated in patients with NYHA Class IV HF or NYHA Class II-III HF with recent decompensation requiring hospitalization or referral to a specialized HF clinic
  - > twofold increase in mortality in HF patients
- Side Effects
  - GI, skin disorders
  - Can prolong QTc but low risk of Torsades
  - Interferes with digoxin metabolism

Concern: LIVER Dysfunction: 1/2011

ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class II A Recommendation:
Dronedarone is reasonable to decrease the need for hospitalization for cardiovascular events in patients with paroxysmal AF or after conversion of persistent AF. Dronedarone can be initiated during outpatient therapy (Level of Evidence: B)

Reduces risk of recurrent atrial fibrillation after cardioversion by 25%
ACCF/AHA/HRS Atrial Fibrillation Guidelines

Class III Recommendation:
Dronedarone should not be administered to patients with class IV heart failure or patients who have had an episode of decompensated heart failure in the past 4 weeks, especially if they have depressed left ventricular function (left ventricular ejection fraction 35%) (Level of Evidence: B)
More on Dronederone

♥ PALLAS Trial
- Dronederone in **permanent atrial fibrillation**
- **Stopped early** due to adverse outcomes in dronederone arm
- Adverse outcomes were cardiovascular in nature and not hepatic in nature

Preventing Thromboembolism

♥ Consideration in all patients with atrial fibrillation of atrial flutter based on stroke risk

♥ Warfarin established as gold standard
- Eliminates excess rates of ischemic stroke, reduces stroke severity and reduces post stroke mortality
- Target INR of 2.0-3.0
- Superior to ASA and ASA plus clopidogrel
- Warfarin in atrial fibrillation in stable CAD
- Warfarin in atrial fibrillation post ACS / PCI
Important Nursing Consideration in Oral Anticoagulation:

HTN Control to Reduce the Risk of Cerebral Hemorrhage

Dabigatran (Pradaxa)

♥ Oral direct thrombin inhibitor
  • Is a prodrug (dabigatran etexilate) that is converted in liver to active form
  • Peak plasma levels in 1.5 hours; half-life 12 to 18 hours
  • Eliminated mostly by kidneys (reduced dose for moderate renal failure, not recommended in severe renal failure)

♥ Predictable dose-response relationship so no lab monitoring of coagulation status needed

♥ Drug to drug interactions exist

♥ Dose:
  • 150 mg PO BID
  • 75 mg PO BID with creatinine clearance 15 to 30 mL/minute
    – These patients and this dose not tested in clinical trials
Dabigatran

♥ RE-LY trial (Connolly et al, 2009)
♥ Study results (stroke / systemic embolism) compared to warfarin:
  • 110 mg BID non-inferior to warfarin (p < 0.001)
  • 150 mg BID superior to warfarin (p< 0.001)
♥ Rate of major bleeding
  • 110 mg BID lower than warfarin (p=0.003)
  • 150 mg BID no different from warfarin dose of dabigatran (p=0.31)
    – One area of concern GI Bleed
♥ Ischemic stroke
  • Statistically lower with dabigatran at 150 mg PO BID
♥ Hemorrhagic stroke
  • Statistically lower with dabigatran at both doses (p < 0.001).
♥ Approved for reduction of stroke in patients with AF at intermediate or high risk of stroke.
♥ Specific patient characteristics
  • 30.9% to 32.6% CHADS2 score = 0-1
  • 34.7% to 37.0% CHADS2 score = 2

Rivaroxaban (Xarelto)

♥ Oral direct factor Xa inhibitor
  • Maximum plasma level in 3 hours
  • Half-life 5-9 hours (up 11 to 13 hrs if > 75 years old)
  • Dose 20 mg PO daily
  • Should be taken with food
  • Hepatic and renal excretion
    – Contraindicated in severe renal failure
♥ Predictable dose-response relationship
  so no lab monitoring needed
Rivaroxaban

♥ ROCKET AF (Patel et al., 2011)
  • Double-blind randomized trial
  • 14,264 patients with nonvalvular atrial fibrillation (at increased risk for stroke)
  • Mean CHADS2 score 3.5
    – 87% to 86.9% had CHADS2 score > 3
  • Rivaroxaban (at a daily dose of 20 mg) or dose-adjusted warfarin
  • Composite of stroke (ischemic or hemorrhagic) and systemic embolism
  • P<0.001 for non-inferiority of rivaroxaban
  • No significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group

Apixaban (Eliquis)

♥ Oral factor Xa inhibitor
♥ Rapid absorption; 8 to 15 hour elimination ½ life
♥ 25% renal excretion
♥ Dose: 5 mg BID
♥ Dose: 2.5 mg BID
  • Creatinine > 1.5 mg/dL and either
  • Age > 80 years
  • Weight ≤ 60 kg
Apixaban

♥ ARISTOTLE (Granger et al., 2011.)
♥ Randomized, double blind, double dummy
♥ 18,201 patients; median age 70 years; 35% female
♥ Apixaban 5 mg BID versus warfarin (INR 2.0 to 3.0)
  • 2.5 mg BID used in subset of patients
♥ Primary objective evaluated for non-inferiority for primary endpoint of ischemic stroke/ hemorrhagic stroke / systemic embolism
  • Found to be non inferior to warfarin (p < 0.001)
♥ Secondary objective evaluated for superiority for primary endpoint of ischemic stroke/ hemorrhagic stroke / systemic embolism
  • Found to be superior to warfarin (p= 0.01)
♥ Primary safety outcome: Major bleeding
  • Statistically less with apixaban (p<0.001)
♥ Delayed by FDA for review of data management and verification
♥ No statistical difference in ischemic stroke.

Edoxaban

♥ ENGAGE AF-TIMI 48
♥ Randomized, double-blind, double-dummy trial
♥ 21,105 patients, follow up 2.8 years
♥ Tested for non-inferiority for stroke or systemic embolism
♥ P = < 0.001 for high dose and P = 0.005 for low dose
♥ Significantly lower rates of bleeding and cardiovascular death compared to warfarin at both doses
More on Factor Xa Inhibitors

♥ PT may provide qualitative assessment of presence of factor Xa
♥ Not sensitive for quantitative anticoagulation effect
♥ Point of care INR should not be used to gauge anticoagulation effects
♥ Chromogenic assay can provide quantitative assessment – not widely available, not fully studied, not recommended at this time
♥ Not all drug to drug interactions are known
♥ Factor Xa inhibitor antidote, andexanet alfa – breakthrough therapy designation by FDA

Electrical Cardioversion

♥ Direct current cardioversion
♥ Involves delivery of an electrical shock synchronized with the intrinsic activity of the heart
♥ Usually is done by sensing R wave on the EKG.
Electrical Cardioversion

♥ Assures no electrical stimulation from 60–80 ms before to 20-30 ms after the apex of the T wave
  • vulnerable phase of cardiac cycle
♥ Used to normalize all abnormal cardiac rhythms except for ventricular fibrillation or pulseless VT
♥ Rhythms due to re-entry are more suitable for cardioversion
♥ Rhythms due to automaticity do not respond to cardioversion

Electrical Cardioversion

♥ Often performed electively
♥ Need for anesthesia
♥ Immediate need for hemodynamically unstable rhythms
♥ Anticoagulation prophylaxis (same with pharmacological cardioversion)
♥ Full anticoagulation versus TEE / Heparin strategy
♥ Risk for thromboembolism greatest when atrial fibrillation present greater than 48 hours
Indications for Emergent DC Cardioversion

♥ Active ischemia
♥ Symptomatic hypotension
♥ Severe heart failure
♥ Preexcitation via an accessory pathway

Contraindicated in presence of digitalis toxicity or hypokalemia

Example of WPW Atrial Fib
(antegrade conduction via accessory pathway)
Echo Contrast

♥ This is a pre-thrombosis state in which the enlarged/inefficient atrium allows blood flow to become sluggish, with the RBC's visible as swirling "smoke" under echo imaging. The slowly moving blood has the potential to form thrombus, especially in the crescent shaped atrial appendage.
Electrical Cardioversion: Technical Issues

- Need for good R wave and good P wave visualization
- AP placement preferred (short axis)
- Initial energy delivered (monophasic) for atrial flutter may be as low as 50 J
- Higher energy is needed for atrial fibrillation starting at least 200 J
- Initial higher energy produces more immediate success and may reduce total energy delivered
- Maximum J is 400
- Biphasic waveforms use less energy
- Time between shocks not less than one minute
Treatment: Electrical Cardioversion

♥ Factors Predicting Success:
♥ Short duration of atrial fibrillation
♥ Atrial flutter
♥ Young Age

♥ Factors Predicting Failure:
♥ Left atrial enlargement
♥ Underlying heart disease
♥ Cardiomegaly

Success rates vary from 70% to 90%

The relapse rate is high without continuation of antiarrhythmic drug therapy

Cardioversion in Patients with Devices

♥ Can be safe when appropriate precautions are taken
♥ Generators are designed to protect themselves but programmed data can still be altered
♥ Device should be interrogated before and after procedure

♥ Electricity conducted along an implanted lead can cause myocardial damage leading to exit block and failure of ventricular capture
♥ Paddle should be positioned away from implanted devices
♥ Internal cardioversion does not interfere with pacemaker function
Nursing Considerations in Cardioversion

♥ Emergency cart
  • Intubation supplies / ambu bag
  • Emergency drugs (lidocaine, epinephrine, amiodarone, atropine)
♥ Sedation reversal agent
♥ O₂ delivery equipment
♥ Suction equipment
♥ O₂ saturation monitor, and non-invasive BP monitoring equipment

Electrical Cardioversion

♥ Complications
  • Embolism (1%-7% without prophylactic anticoagulation)
  • Benign arrhythmias
  • Ventricular arrhythmias with hypokalemia and digitalis toxicity
  • Myocardial damage has not been confirmed
  • Reoccurrence of atrial fibrillation
    – Prophylactic antiarrhythmic drug therapy before cardioversion for patients at risk
Pharmacological Cardioversion

♥ Works best if AF present for < 7 days
♥ Most effective drugs are
  • Ibutilide (Corvert)
  • Flecainide (Tambocor)
  • Dofetilide (Tycosin)
  • Propafenone (Rhythmol)
  • Amiodarone
♥ Associated with side effects
  • Bradycardia (8%)
  • QT prolongation (1.5%)
  • Ventricular arrhythmias (1.3%)

Recommendations for Pharmacological Cardioversion of Atrial Fibrillation

♥ Administration of flecainide, dofetilide, propafenone, or ibutilide is recommended for pharmacological cardioversion of AF
♥ Class IIa recommendations:
  • Amiodarone
  • “Pill-in-the-pocket” single oral dose of propafenone or flecainide to terminate persistent AF outside the hospital in selected patients (no sinus node or AV node dysfunction, LQT, Brugada, or structural heart disease)
Ablation for AF

♥ Paroxysmal AF is triggered by ectopic foci localized to the PVs in about 90% of patients with structurally normal hearts
  • Most patients have one or two foci 2 to 4 cm inside the pulmonary veins (the remaining foci are usually in the right or left atrium)
  • Pulmonary vein isolation procedure is successful in 60% to 70%

♥ Patients cardioverted from permanent AF often have multiple ectopic sites in both atria
  • More difficult to ablate multiple foci successfully

Pulmonary Vein Isolation Procedures

♥ Focus on isolating the triggers in the PVs from the left atrial myocardium
  • **Segmental ostial ablation** targets isolated sites of ectopic foci in PVs and ablates the connection between those sites and atrial myocardium
  • **Circumferential ablation** creates lesions that encircle the ostia of all four pulmonary veins and completely isolates them from atrial myocardium – most common procedure
Complications of PV Isolation

- Cardiac tamponade
- Pulmonary vein stenosis (can lead to pulmonary hypertension)
- Esophageal injury or atrio-esophageal fistula
- Phrenic nerve injury
- Thromboembolism
- Mitral valve trauma
- Radiation exposure due to long procedures

Ablation for Atrial Fibrillation

Potential energy sources:
- Radiofrequency (heats tissue)
- Cryothermy (freezes tissue)
- Focused ultrasonography
Guideline Update

Catheter ablation is useful in patients with symptomatic, paroxysmal AF who have not responded to or tolerated antiarrhythmic medications (Class I).

Guideline Update

Catheter ablation is also reasonable in selected patients with symptomatic, paroxysmal AF prior to a trial of medical therapy, provided that it can be performed at an experienced center (Class IIa).
AV Node Ablation

♥ Creates complete AV block to prevent conduction of AF into ventricles (requires insertion of permanent pacemaker)

Ablation for Permanent Atrial Fibrillation
Cox-Maze III

♥ “Cut & sew” method developed in 1987
• Considered the gold standard for surgical treatment of AF
• Isolates the pulmonary veins
• Isolate the posterior left atrium
• Interrupts the macro reentrant circuits responsible for atrial fibrillation and atrial flutter
• Amputates the left atrial appendage

Creates a pathway from sinus node to AV node and allows all of atrium to be activated
Technical challenges of procedure limited its use.

Cox-Maze IV Using Ablation

♥ Creation of lesions using ablation technology

- Unipolar or bipolar energy sources
- Unipolar
  - Unipolar radiofrequency (RF) (heats tissue)
  - Cryothermia (freezes tissue)
  - High frequency ultrasound
- Bipolar
  - Bipolar radiofrequency (RF)
  - Delivered between two electrodes held in place inside a jaw like clamp
Cox-Maze IV Using Ablation

- Must create transmural lesions from epicardial or endocardial surface
  - Unipolar sources don’t consistently create transmural lesion
  - Unipolar cryosurgery or radiofrequency ablation can also cause unintended cardiac injury

- Bipolar RF clamps most widely used device
  - Limitation: Only tissue fitting between clamp can be ablated, particularly limiting when performed on beating heart
  - Right atrial isthmus and left atrial isthmus are not able to be fully ablated

Role of the Isthmus

Right Atrial Isthmus

Left Atrial Isthmus

Performed through median sternotomy or right mini thoracotomy with patient on CPB

Uses combination of unipolar and bipolar RF or cryothermia ablations delivered through small atrial incisions to achieve desired lesions

Left atrial appendage is also amputated

Results similar to Cox-Maze III

The term “Maze” procedure implies entire bi-atrial lesion set of the Cox-Maze procedure (includes ablation of both the right and left atrial isthmuses)

Surgical Procedures for Atrial Fibrillation

Cox-Maze IV: Cox-Maze III lesion set using ablation technology

Pulmonary vein isolation

Pulmonary vein isolation with a left atrial lesion set connecting to the mitral valve annulus

Amputation of left atrial appendage
Usually done in conjunction
Percutaneous Left Atrial Appendage Occlusion

♥ The LAA is a multi-lobed structure of variable anatomy that is attached to the LA
♥ More than 90% of clots in patients with non-rheumatic AF form in the LAA
♥ Many patients are unable to take coumadin and are at risk for stroke in chronic AF
♥ Mechanical occlusion of LAA can prevent thrombus embolization

LAA Occlusion Devices

- Watchman
- Amplatzer
LAA Occlusion Devices: Watchman

♥ Protect AF Trial
  • 2009: Non inferior but safety concern: Pericardial effusion
  • May 2013: New long term data (45 month follow up of 800 patients) superior to warfarin with respect to all-cause and CV mortality and hemorrhagic stroke in patients with nonvalvular atrial fibrillation and stroke risk factors

♥ Prevail Trial – 2013
  • Did not meet 1st primary endpoint
    – Non inferiority to warfarin for composite of stroke, systemic embolism, or cardiovascular or unexplained death
  • Met 2nd primary endpoint
    – Non inferiority to warfarin for prevention of ischemic stroke or systemic embolism

♥ FDA status
  • 2010 FDA denied approval
  • December 2013 – advisory board 13 to 1 recommended approval

LAA Occlusion Devices: Amplatzer

♥ AMPLATZER Cardiac Plug
♥ European CE Mark Approval January 2013
♥ The AMPLATZER™ Cardiac Plug Clinical Trial (ACP Trial)
  • First patient enrolled in March 2013
From Chaos to Clarity

Atrial Fibrillation Clinical Considerations: Case Examples

38 year old female with palpitations and light headedness

No past medical history

Monitor – AVNRT and infrequent short (seconds) runs atrial fibrillation

AVNRT associated with symptoms. Atrial fibrillation incidental finding.

Options?

86 year old male presenting with TIA symptoms.

Found in atrial fibrillation of unknown origin.

History of HTN and debilitating arthritic pain and spinal stenosis.

Options?
Reflection and Gratitude

A Final Thought

Impact every patient and family on their journey and provide safe passage by meeting them where they are, connecting with them in a meaningful way, and delivering care with wisdom and intention.

- Karen
BE THE BEST THAT YOU CAN BE EVERY DAY. YOUR PATIENTS ARE COUNTING ON IT!

karen@cardionursing.com

Final slides will be available at www.cardionursing.com next week